4/14/05

ANSWER 1 OF 1 CASREACT COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 141:225319 CASREACT
TITLE: Process for preparation of N-heteroaryl-N-aryl-amines
INVENTOR(S): Snoonian, John R.; Oliver-Shaffer, Patrica-Ann
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C07D213-80
SECONDARY: C07D213-79; C07D213-75; C07C273-18; C07C275-42; C07C275-30
CLASSIFICATION: 27-16 (Heterocyclic Compounds (One Hetero Atom))
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004072038 | A1 | 20040826 | WO 2004-US3933 | 20040210 |

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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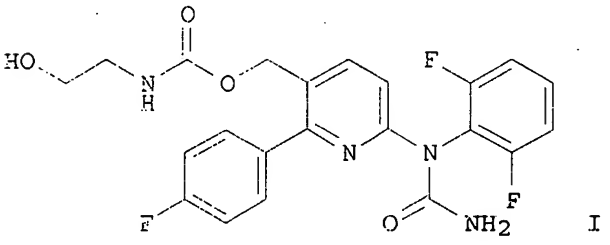
|---|---|---|---|---|
| US 2004230058 | A1 | 20041118 | US 2004-775687 | 20040210 |
| PRIORITY APPLN. INFO.: | | | US 2003-446641P | 20030210 |
| | | | US 2003-474272P | 20030528 |

OTHER SOURCE(S): MARPAT 141:225319
GRAPHIC IMAGE:



I

ABSTRACT:
The present invention relates to a process for producing diarylamine derivs. with general formula of Ar1-NH-Ar2 [wherein Ar1 and Ar2 = independently (un)substituted aryl or heteroaryl] or salts thereof, which comprises coupling a compound of formula Ar1-X [where X = a leaving group] with an amine of formula Ar2-NH-Y [where Y = CO2Z; Z = alkyl, PhCH2, Fmoc, etc.] in the presence of an ***alkali*** **metal** salt or a transition metal catalyst. For example, the compound I was prepared starting from 6-chloro-2-(4-fluorophenyl)nicotinic acid Me ester (preparation given) and N-(tert-butoxycarbonyl)-2,6-difluoroaniline.

SUPPL. TERM: prepn hetero aryl amine coupling reaction catalyst base

INDEX TERM: Amines, preparation
ROLE: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(diamines, aromatic; preparation of N-heteroaryl-N-aryl-amines)
INDEX TERM: Coupling reaction
(preparation of N-heteroaryl-N-aryl-amines)
INDEX TERM: Transition metals, uses
ROLE: CAT (Catalyst use); USES (Uses)
(preparation of N-heteroaryl-N-aryl-amines)
INDEX TERM: **Alkali metal** salts
ROLE: RGT (Reagent); RACT (Reactant or reagent)
(preparation of N-heteroaryl-N-aryl-amines)
INDEX TERM: Bases, reactions
ROLE: RGT (Reagent); RACT (Reactant or reagent)
(preparation of N-heteroaryl-N-aryl-amines)
INDEX TERM: Coupling reaction catalysts
(transition metals; preparation of N-heteroaryl-N-aryl-amines)
INDEX TERM: 40134-18-7P 210161-08-3P 223760-99-4P 250123-28-5P 745833-06-1P 745833-08-3P 745833-10-7P 745833-21-0P
ROLE: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of N-heteroaryl-N-aryl-amines)
INDEX TERM: 7440-05-3, Palladium, uses
ROLE: CAT (Catalyst use); USES (Uses)
(preparation of N-heteroaryl-N-aryl-amines)
INDEX TERM: 745833-13-0P 745833-15-2P 745833-23-2P
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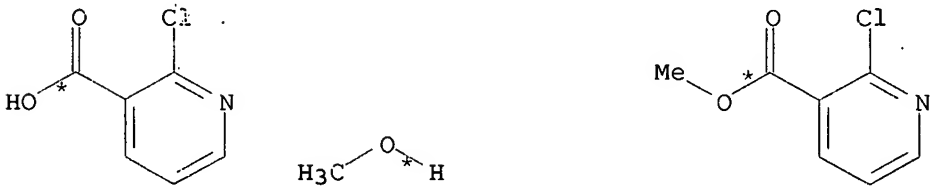
(preparation of N-heteroaryl-N-aryl-amines)
INDEX TERM: 503-38-8, Diphosgene 1336-21-6, Ammonium hydroxide 1765-93-1, 4-Fluorophenylboronic acid 2942-59-8, 2-Chloronicotinic acid 745833-17-4 745833-19-6
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(preparation of N-heteroaryl-N-aryl-amines)
INDEX TERM: 497-19-8, Sodium carbonate, reactions 534-17-8, Cesium carbonate 584-08-7, Potassium carbonate 865-47-4 865-48-5 1310-73-2, Sodium hydroxide, reactions 7440-09-7D, Potassium, salts 7440-17-7D, Rubidium, salts 7440-46-2D, Cesium, salts 7647-01-0, Hydrogen chloride, reactions 7778-53-2, Potassium phosphate
ROLE: RGT (Reagent); RACT (Reactant or reagent)
(preparation of N-heteroaryl-N-aryl-amines)

RX(1) OF 37 A + B ===> C...




A B C

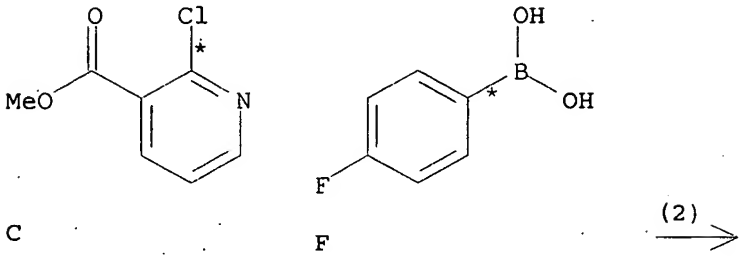
RX(1) RCT A 2942-59-8

STAGE(1)
RGT D 7719-09-7 SOCl2

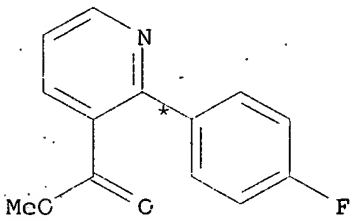
SOL 75-09-2 CH2Cl2

STAGE(2)
RCT B 67-56-1
PRO C 40134-18-7

RX(2) OF 37 ...C + F ===> G...



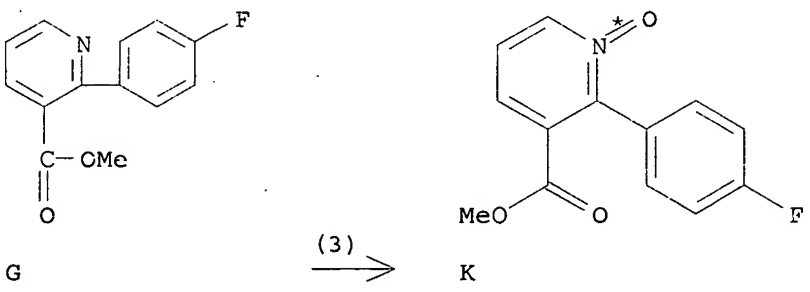

C F




G

RX(2) RCT C 40134-18-7, F 1765-93-1
RGT H 497-19-8 Na2CO3
PRO G 210161-08-3
CAT 14221-01-3 Pd(PPh3)4
SOL 64-17-5 EtOH

RX(3) OF 37 ...G ===> K...




G K

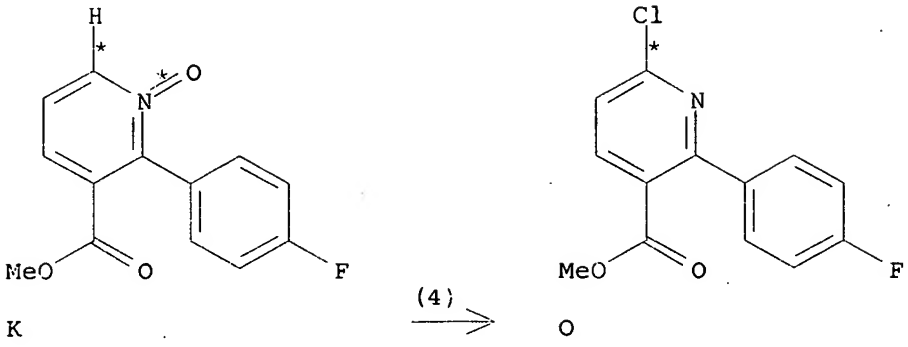
RX(3) RCT G 210161-08-3

STAGE(1)
RGT L 124-43-6 Urea-H2O2, M 64-19-7 AcOH
SOL 7732-18-5 Water

STAGE(2)
SOL 7732-18-5 Water

PRO K 223760-99-4
NTE workup

RX(4) OF 37 ...K ===> O...



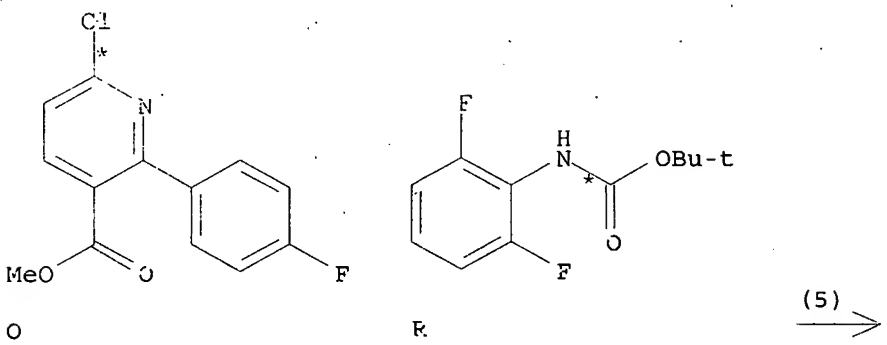

K O

RX(4) RCT K 223760-99-4

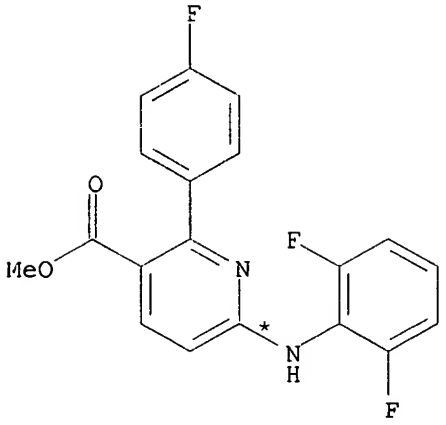
STAGE(1)
RGT P 10025-87-3 POCl3
SOL 107-06-2 ClCH2CH2Cl

STAGE(2)
RGT N 7732-18-5 Water
PRC O 745833-06-1

RX(5) OF 37 ...O + R ===> S...




O R



S

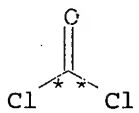
RX(5)

STAGE(1)
RGT T 98327-87-8 Phosphine, [1,1'-binaphthalene]-2,2'-diylbis[diphenyl-
CAT 3375-31-3 Pd(OAc)2
SOL 108-88-3 PhMe

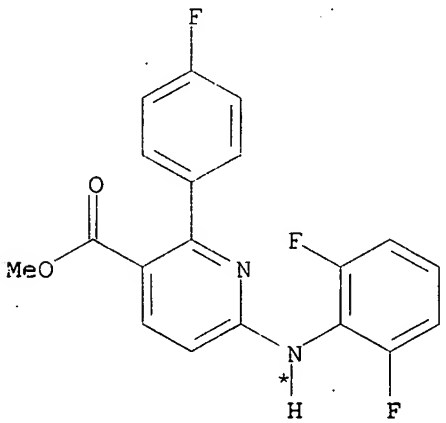
STAGE(2)
RCT O **745833-06-1**, R **745833-17-4**
RGT U 7778-53-2 K3PO4

STAGE(3)
RGT V 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2
PRO S **745833-08-3**
NTE workup

RX(6) OF 37 ...Y + S ===> Z...



Y



S

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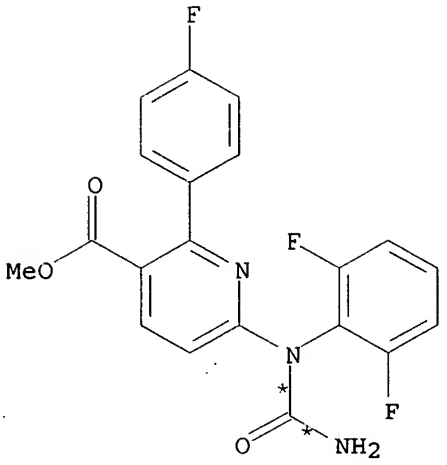
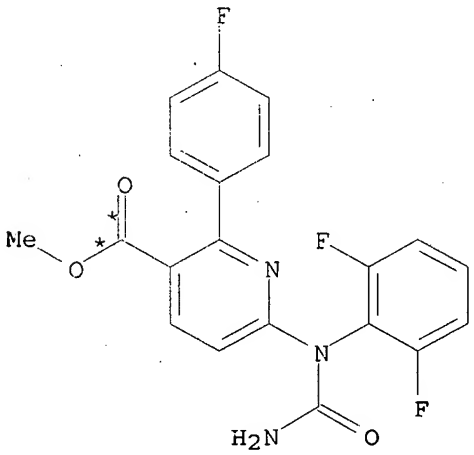


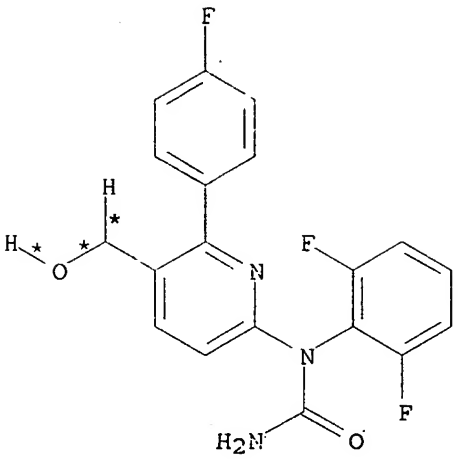
Z

RX(6) RCT Y 75-44-5, S 745833-08-3
RGT AA 7727-37-9 N2
PRO Z 745833-10-7
SOL 108-88-3 PhMe

RX(7) OF 37 ...Z ===> AB...



Z (7) →



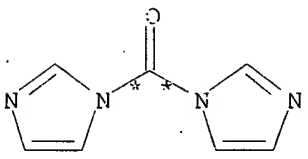
AB
YIELD 80%

RX(7)  RCT  Z 745833-10-7

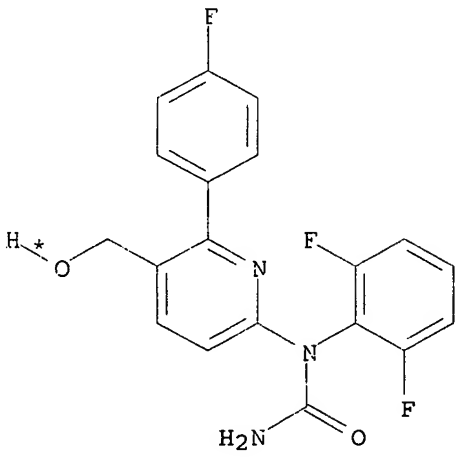
STAGE(1)
RGT  AC 1191-15-7 AlH(Bu-i)2
SOL  109-99-9 THF

STAGE(2)
RGT  AD 7664-93-9 H2SO4
SOL  7732-18-5 Water
PRO  AB 250123-28-5

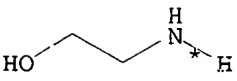
RX(8) OF 37  ...AF + AB + AG ===> AH



AF

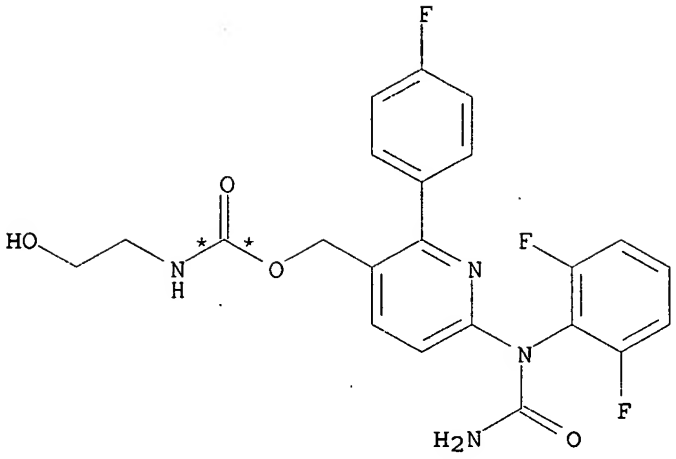


AB



AG

(8) →



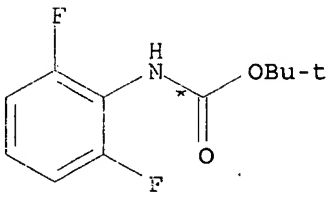
AH

RX(8) RCT AF 530-62-1, AB 250123-28-5

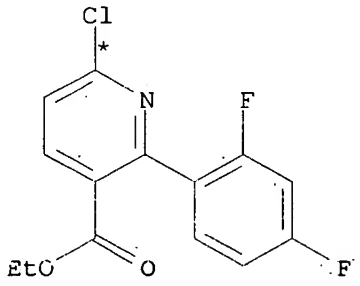
STAGE(1)
SOL 109-99-9 THF

STAGE(2)
RCT AG 141-43-5
SOL 75-05-8 MeCN
PRO AH 745833-13-0

RX(9) OF 37 **R + AJ ===> AK**

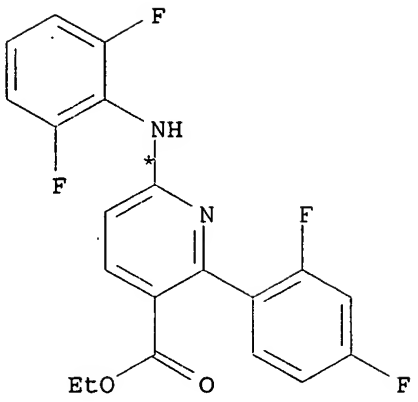


R



AJ

(9) →



● HCl

AK
YIELD 71%

RX(9) RCT R **745833-17-4**, AJ **745833-19-6**

STAGE(1)
RGT AL 534-17-8 Cs2CO3
SOL 872-50-4 NMEP

STAGE(2)
SOL 7732-18-5 Water

STAGE(3)
RGT V 76-05-1 F3CCO2H
SOL 7732-18-5 Water
PRO AK **745833-15-2**

=> d l4 1-4 iall

L4 ANSWER 1 OF 4 CASREACT COPYRIGHT 2005 ACS on STN
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CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES,
ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN,
IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC,
LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX,
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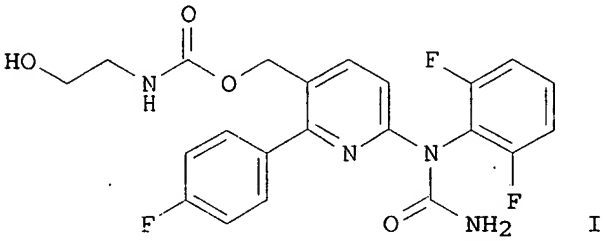

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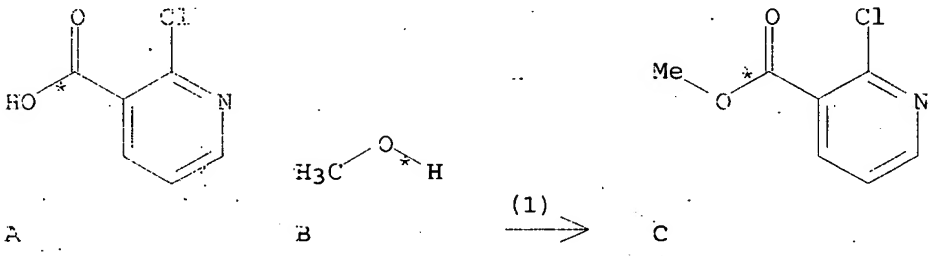
ROLE: RGT (Reagent); RACT (Reactant or reagent)
(preparation of N-heteroaryl-N-aryl-amines)

RX(1) OF 37 A + B ===> C...



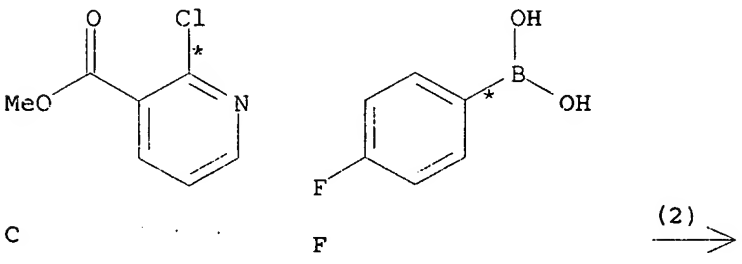

A B C

RX(1) RCT A 2942-59-8

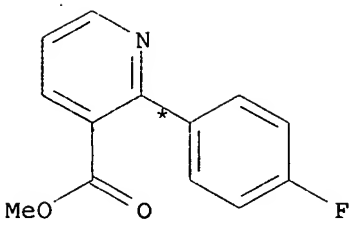
STAGE(1)
RGT D 7719-09-7 SOCl2
SOL 75-09-2 CH2Cl2

STAGE(2)
RCT B 67-56-1
PRO C 40134-18-7

RX(2) OF 37 ...C + F ===> G...



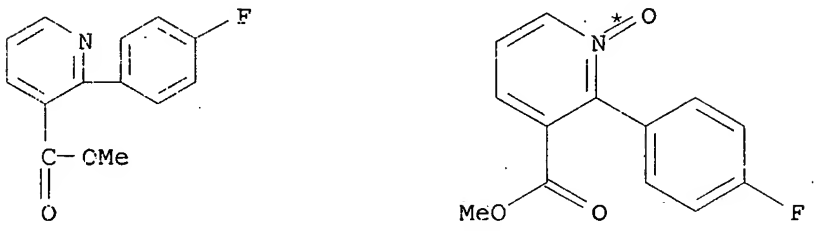

C F



G

RX(2) RCT C 40134-18-7, F 1765-93-1
RGT H 497-19-8 Na2CO3
PRO G 210161-08-3
CAT 14221-01-3 Pd(PPh3)4
SOL 64-17-5 EtOH

RX(3) OF 37 ...G ===> K...



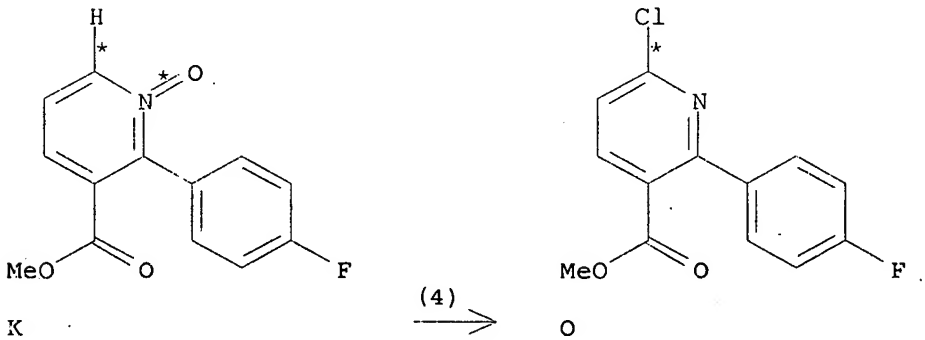
G (3) K

RX(3) RCT G 210161-08-3

STAGE(1)
RGT L 124-43-6 Urea-H2O2, M 64-19-7 AcOH
SOL 7732-18-5 Water

STAGE(2)
SOL 7732-18-5 Water
PRO K 223760-99-4
NTE workup

RX(4) OF 37 ...K ===> O...



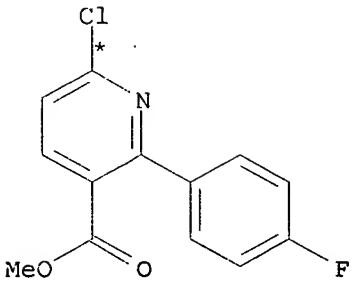
K (4) O

RX(4)  RCT  K 223760-99-4

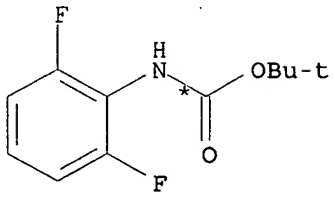
STAGE(1)
RGT  P 10025-87-3 POCl3
SOL  107-06-2 ClCH2CH2Cl

STAGE(2)
RGT  N 7732-18-5 Water
PRO  O 745833-06-1

RX(5) OF 37  ...O + R ===> S...

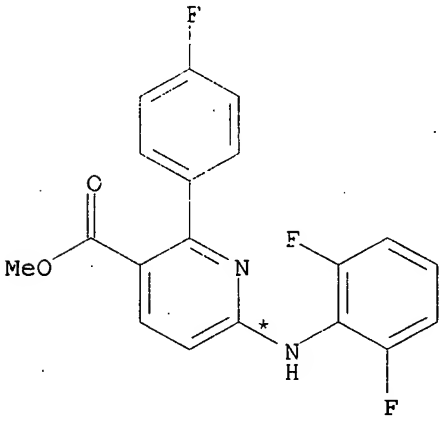



O




R

(5)




S

RX(5)

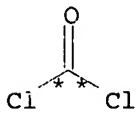
STAGE(1)
RGT  T 98327-87-8 Phosphine, [1,1'-binaphthalene]-2,2'-diylbis[diphenyl-
CAT  3375-31-3 Pd(OAc)2
SOL  108-88-3 PhMe

STAGE(2)
RCT  O **745833-06-1**, R **745833-17-4**
RGT  U 7778-53-2 K3PO4

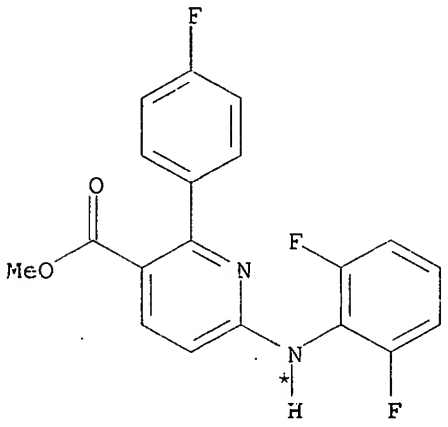
STAGE(3)
RGT  V 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2
PRO S 745833-08-3
NTE workup

RX(6) OF 37 ...Y + S ===> Z...

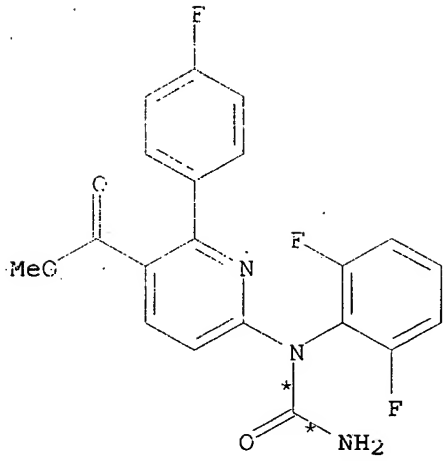


Y



S

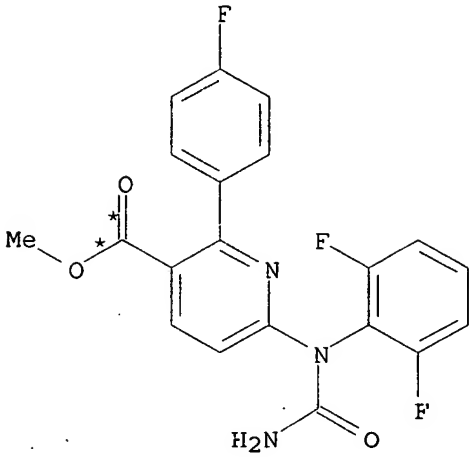
(6)



Z

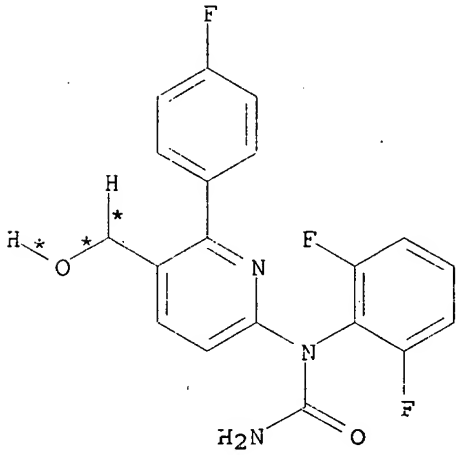
RX(5) RCT Y 75-44-5, S 745833-08-3
RGT AA 7727-37-9 N2
PRO Z 745833-10-7
SOL 108-88-3 PhMe

RX(7) OF 37 ...Z ===> AB...



Z

(7) →



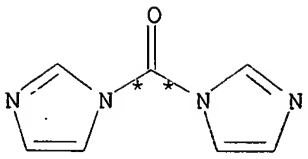
AB
YIELD 80%

RX(7) RCT Z 745833-10-7

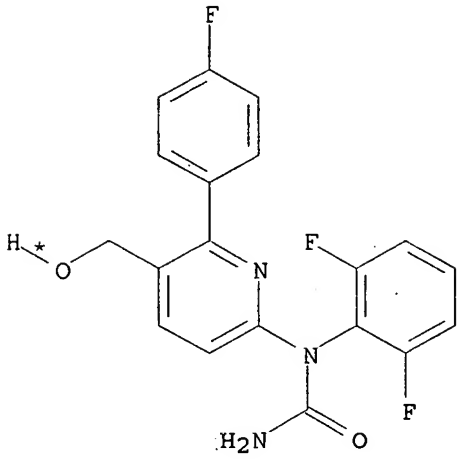
STAGE(1)
RGT AC 1191-15-7 AlH(Bu-i)2
SOL 109-99-9 THF

STAGE(2)
RGT AD 7664-93-9 H2SO4
SOL 7732-18-5 Water
PRO AB 250123-28-5

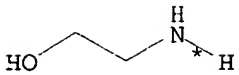
RX(8) OF 37 ...AF + AB + AG ===> AH



AF

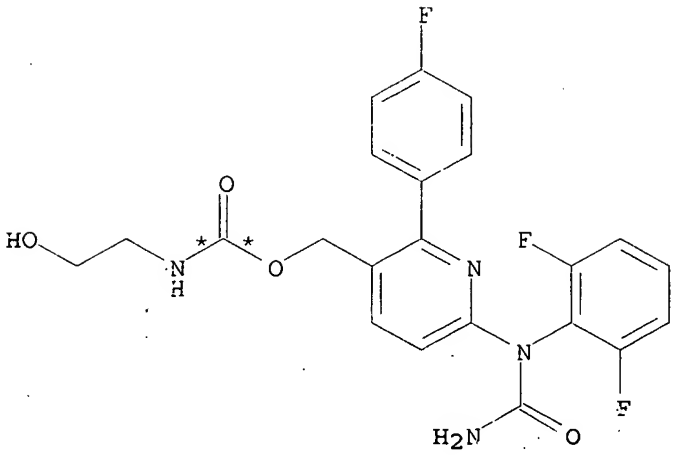


AB



AC

(8) ⟹



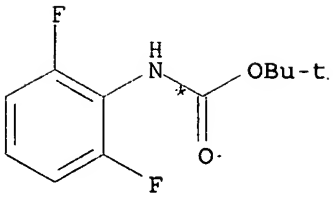
AH

RX(8) RCT AF 530-62-1, AB 250123-28-5

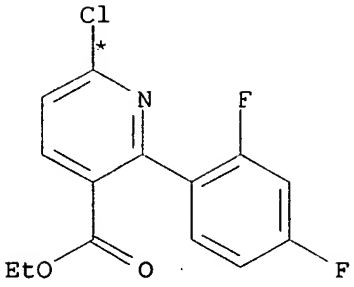
STAGE(1)
SOL 109-99-9 THF

STAGE(2)
RCT AG 141-43-5
SOL 75-05-8 MeCN
PRO AH 745833-13-0

RX(9) OF 37 **R + AJ ===> AK**

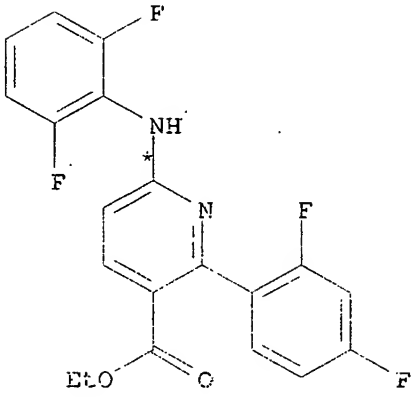


R



AJ

(9) →



● HCl

AK
YIELD: 71%

RX(9) RCT R **745833-17-4**, AJ **745833-19-6**

STAGE(1)
RGT AL 534-17-8 Cs2CO3
SOL 872-50-4 NMEP

STAGE(2)
SOL 7732-18-5 Water

STAGE(3)
RGT V 76-05-1 F3CCO2H
SOL 7732-18-5 Water
PRO AK **745833-15-2**

L4 ANSWER 2 OF 4 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 139:331783 CASREACT
TITLE: Synthesis, spectral and magnetic studies of mononuclear and binuclear Mn(II), Co(II), Ni(II) and Cu(II) complexes with semicarbazone ligands derived from sulfonamide
AUTHOR(S): Saleh, A. A.; Khalil, S. M. E.; Eid, M. F.; El-Ghamry, M. A.

CORPORATE SOURCE: Department of Chemistry, Faculty of Education, Ain Shams University, Cairo, Egypt
SOURCE: Journal of Coordination Chemistry (2003), 56(6), 467-480
CODEN: JCCMBQ; ISSN: 0095-8972
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 78-7 (Inorganic Chemicals and Reactions)
Section cross-reference(s): 1, 10

ABSTRACT:
Mononuclear and binuclear Mn(II), Co(II), Ni(II) and Cu(II) complexes of new semicarbazone ligands derived from sulfonamide were synthesized and characterized by elemental anal. and IR spectra. In mononuclear complexes, the semicarbazone behaves as a monoanionic terdentate or neutral terdentate ligand towards the metal ion. However, in binuclear complexes, it behaves as a monoanionic terdentate towards one of the bivalent metal ions and monoanionic bidentate ligand towards the other metal ion in the same complex. Electronic spectra and magnetic susceptibility measurements of the solid complexes indicated octahedral geometry around Mn(II), Co(II) and Ni(II) and square planar around the Cu(II) ion. These geometries were confirmed by the results obtained from thermal analyses. The antifungal properties of the ligands and their complexes were studied.

SUPPL. TERM: **transition metal** sulfonamide semicarbazone complex prepn; antifungal activity sulfonamide semicarbazone **transition metal** complex; thermal decompn **transition metal** sulfonamide semicarbazone complex

INDEX TERM: Thermal decomposition
(of **transition metal** sulfonamide semicarbazone complexes)

INDEX TERM: Fungicides
(preparation and thermal decomposition of **transition metal** sulfonamide semicarbazone complexes as)

INDEX TERM: **Transition metal** complexes
ROLE: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(sulfonamide semicarbazone; preparation and antifungal activity and thermal decomposition of)

INDEX TERM: 613221-31-1P 613221-32-2P 613221-33-3P 613221-34-4P
ROLE: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation and complexation with **transition metals** and antifungal activity)

INDEX TERM: 7803-57-8, Hydrazine monohydrate 41104-55-6
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(preparation and reactant for preparation of sulfonamide semicarbazones)

INDEX TERM: 87013-80-7P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reactant for preparation of sulfonamide semicarbazones)

INDEX TERM: 613221-35-5P 613221-38-8P 613221-40-2P 613221-43-5P
613221-44-6P 613221-45-7P 613221-46-8P 613221-49-1P
613221-50-4P 613221-53-7P 613221-54-8P 613221-56-0P
613221-57-1P 613221-58-2P 613221-59-3P 613221-62-8P
ROLE: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation and thermal decomposition and antifungal activity of)

INDEX TERM: 63-74-1, 4-Aminobenzenesulfonamide 90-02-8, Salicylaldehyde, reactions 118-93-4 541-41-3, Ethyl chloroformate 552-89-6, 2-Nitrobenzaldehyde
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reactant for preparation of sulfonamide semicarbazones)

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD.


REFERENCE(S):
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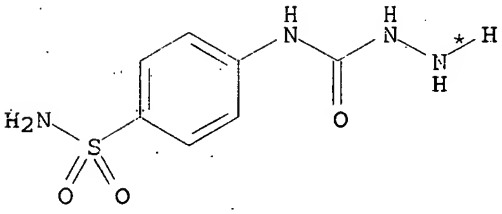
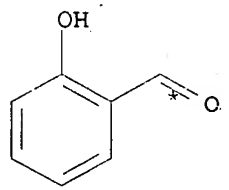
(18) Sonar, G; J Indian Chem Soc 1995, V72, P677
(19) West, D; Coord Chem Rev 1993, V49, P123


RX(1) OF 79 ...A + B ===> C...

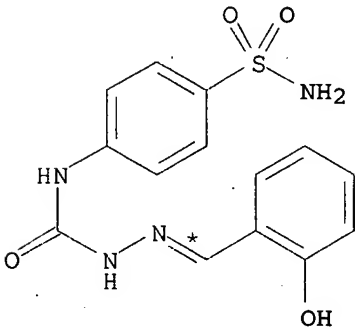


A



B

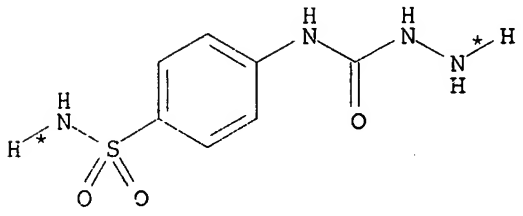
(1)



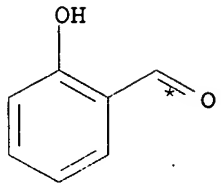
C

RX(1)  RCT  A 87013-80-7, B 90-02-8
PRO  C 613221-31-1
SOL  68-12-2 DMF
NTE  product depends on time of refluxing

RX(2) OF 79  ...A + 2 B ===> E...

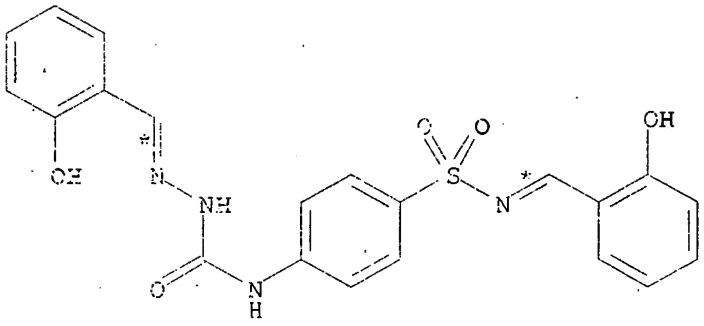


A



2 B

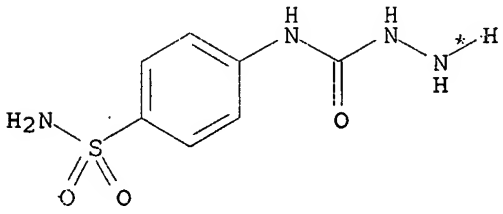
(2) →



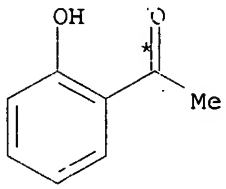
E

RX(2)  RCT  A 87013-80-7, B 90-02-8
PRO  E 613221-32-2
SOL  68-12-2 DMF
NTE  product depends on time of refluxing

RX(3) OF 79  ...A + F ===> G...

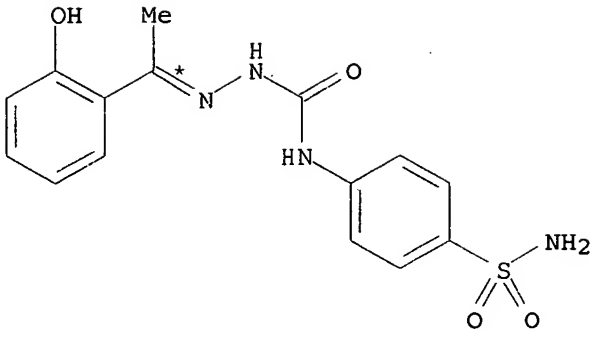


A



F

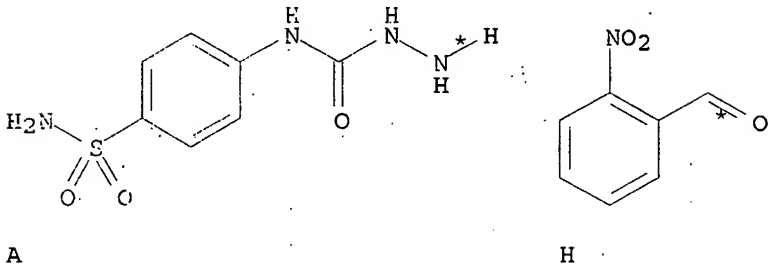
(3) →



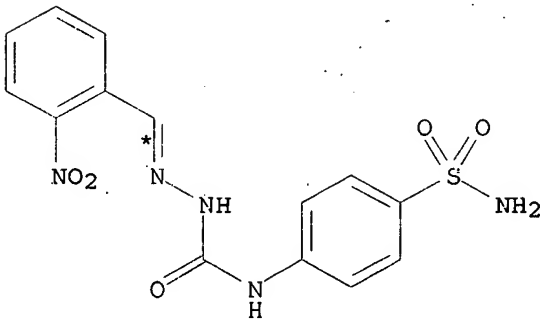
G

RX(3) RCT A 87013-80-7, F 118-93-4
PRO G 613221-33-3
SOL 68-12-2 DMF

RX(4) OF 79 ...A + H ===> I...



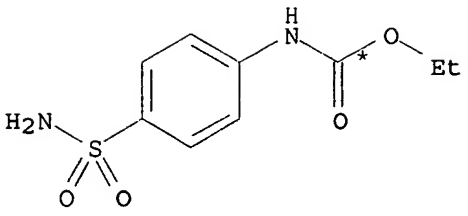
A H (4)



I

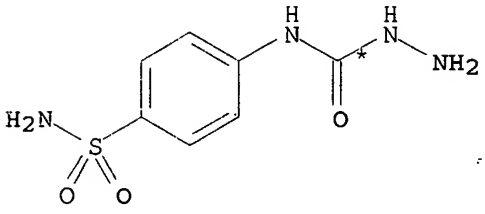
RX(4) RCT A 87013-80-7, H 552-89-6
PRO I 613221-34-4
SOL 68-12-2 DMF

RX(5) OF 79 ...J ===> A...



J

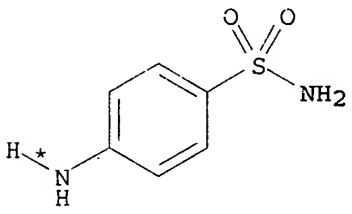
(5) →



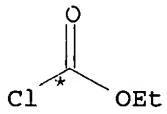
A

RX(5) RCT J 41104-55-6
RCT K 7803-57-8 N2H4-H2O
PRO A 87013-80-7
SOL 68-12-2 DMF

RX(6) OF 79 L + M ===> J...

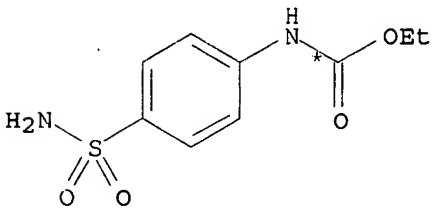


L



M

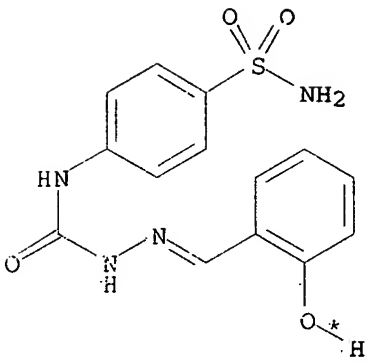
(6) →



J

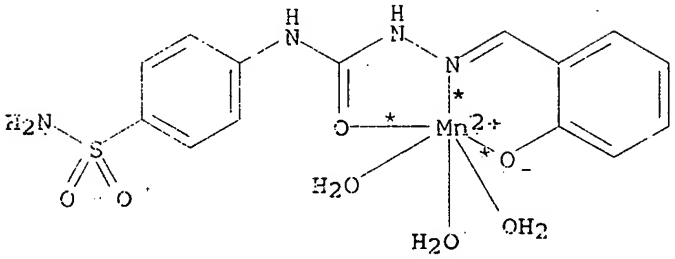
RX(6) RCT L 63-74-1, M 541-41-3
PRO J 41104-55-6
SOL 68-12-2 DMF

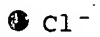
RX(7) OF 79 ...C ===> N

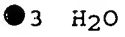


C

(7)







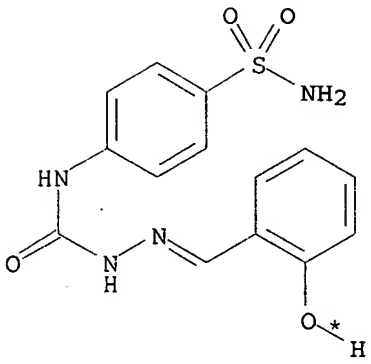
N

RX(7) RCT C 613221-31-1

STAGE(1)
RGT O 1310-65-2 LiOH
SOL 7732-18-5 Water, 64-17-5 EtOH

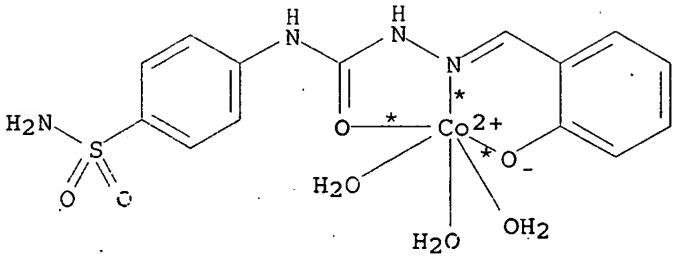
STAGE(2)
RGT P 7773-01-5 MnCl2
SOL 7732-18-5 Water
PRO N 613221-35-5

RX(8) OF 79 ...C ===> S





C (8) S: CM 1



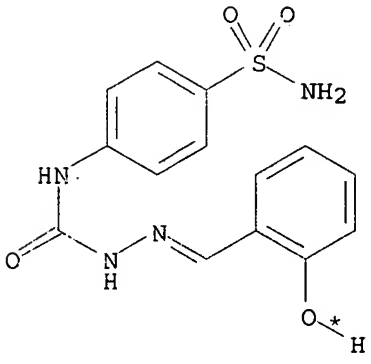
S: CM 2

RX(8) RCT C 613221-31-1

STAGE(1)
RGT O 1310-65-2 LiOH
SOL 7732-18-5 Water, 64-17-5 EtOH

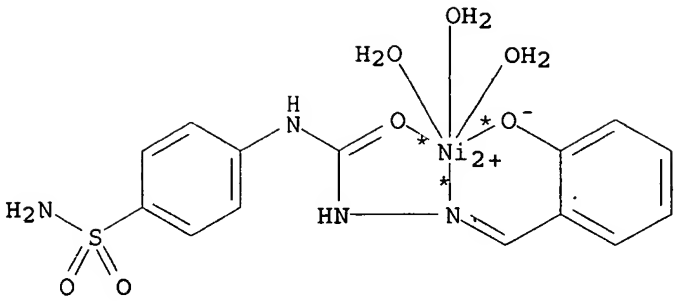
STAGE(2)
RGT T 10141-05-6 Co(NO3)2
SOL 7732-18-5 Water
PRO S 613221-38-8

RX(9) OF 79 ...C + R ===> U



$H_3C-CH_2-OH$ $H_3C-CH_2-OH$

C R (9) U: CM 1



● $Cl^-$

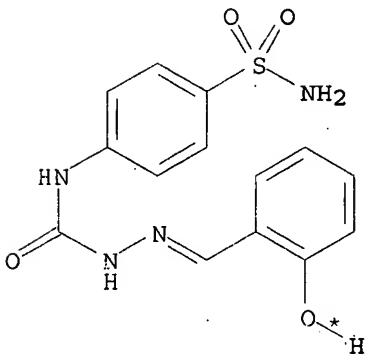
U: CM 2

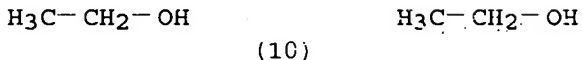
RX(9) RCT C 613221-31-1, R 64-17-5

STAGE(1)
RGT O 1310-65-2 LiOH
SOL 7732-18-5 Water, 64-17-5 EtOH

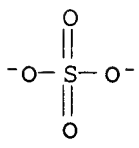
STAGE(2)
RGT V 7718-54-9 NiCl2
SOL 7732-18-5 Water
PRO U 613221-40-2

RX(10) OF 79 ...C + R ===> W

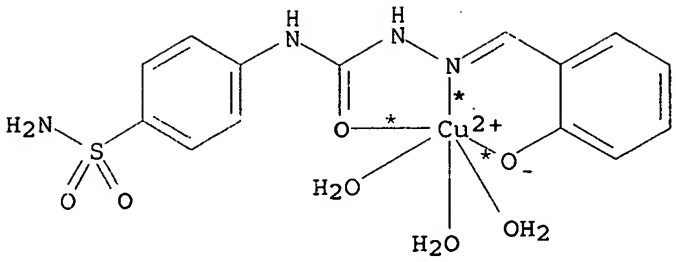




C R (10) W: CM 1



W: CM 2



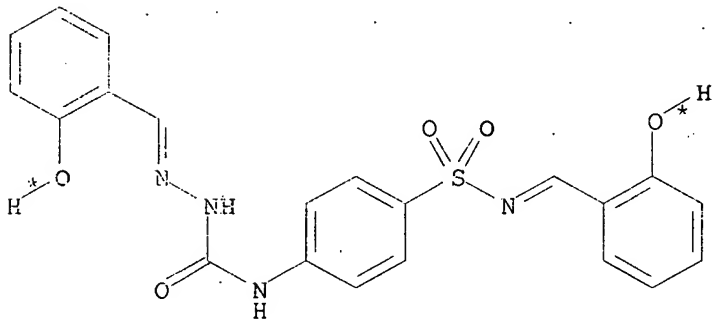
W: CM 3

RX(10) RCT C 613221-31-1, R 64-17-5

STAGE(1)
RGT O 1310-65-2 LiOH
SOL 7732-18-5 Water, 64-17-5 EtOH

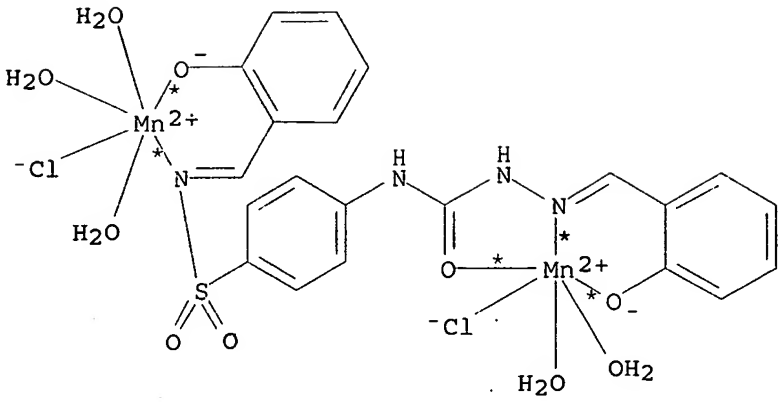
STAGE(2)
RGT X 7758-98-7 CuSO4
SOL 7732-18-5 Water
PRO W 613221-43-5

RX(11) OF 79 ...E ===> Y



E

(11)



● 6 $H_2O$

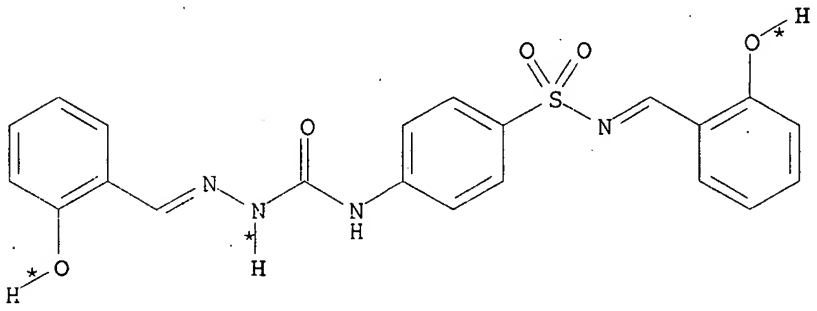
Y

RX(11) RCT E 613221-32-2

STAGE(1)
RGT O 1310-65-2 LiOH
SOL 7732-18-5 Water, 64-17-5 EtOH

STAGE(2)
RGT P 7773-01-5 MnCl2
SOL 7732-18-5 Water
PRO Y 613221-44-6

RX(12) OF 79 ...E ===> Z



E

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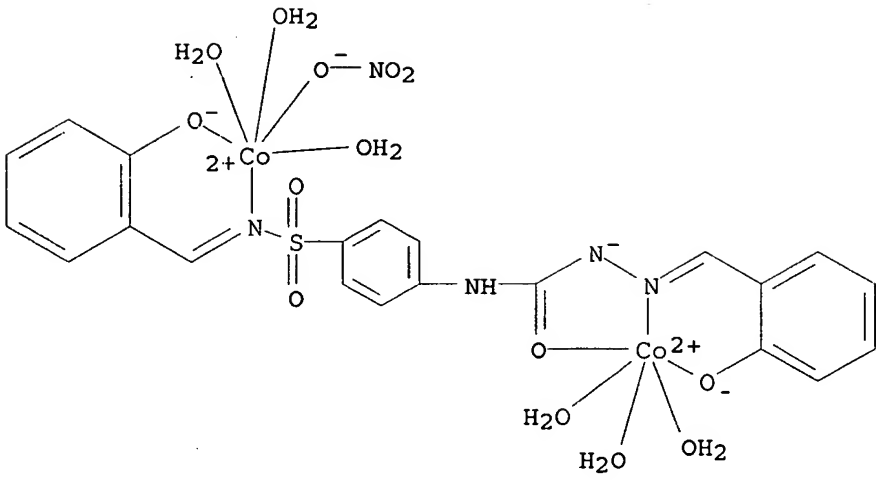


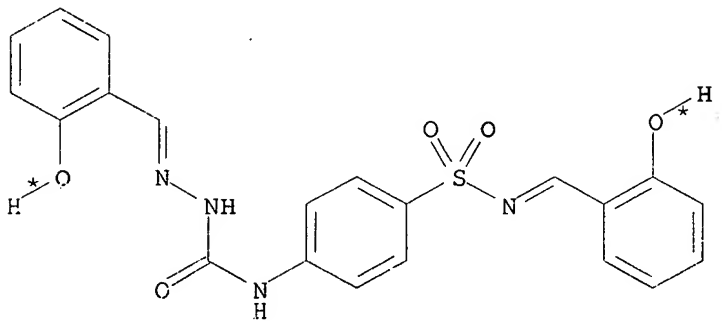
Z

RX(12) RCT E 613221-32-2

STAGE(1)
RGT O 1310-65-2 LiOH
SOL 7732-18-5 Water, 64-17-5 EtOH

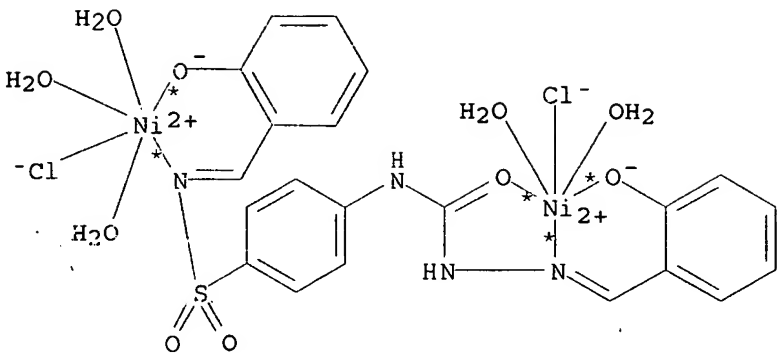
STAGE(2)
RGT T 10141-05-6 Co(NO3)2
SOL 7732-18-5 Water
PRO Z 613221-45-7

RX(13) OF 79 ...E ===> AA



E

(13)



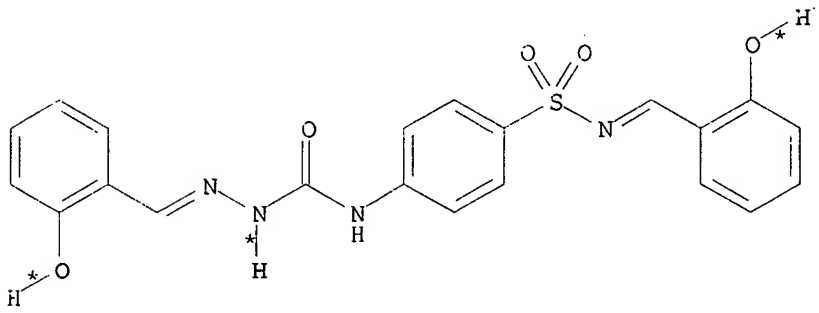
AA

RX(13) RCT E 613221-32-2

STAGE(1)
RGT O 1310-65-2 LiOH
SOL 7732-18-5 Water, 64-17-5 EtOH

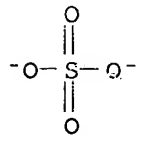
STAGE(2)
RGT V 7718-54-9 NiCl2
SOL 7732-18-5 Water
PRO AA 613221-46-8

RX(14) OF 79 ...E ===> AB

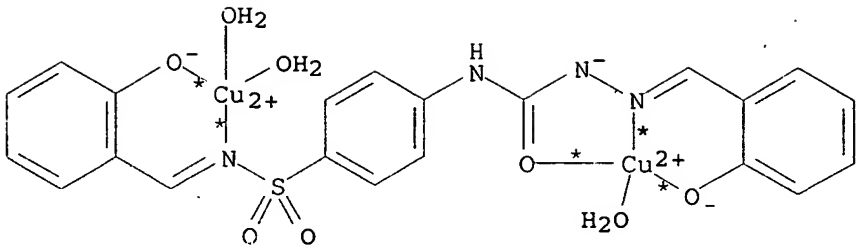


E

(14)



AB: CM 1



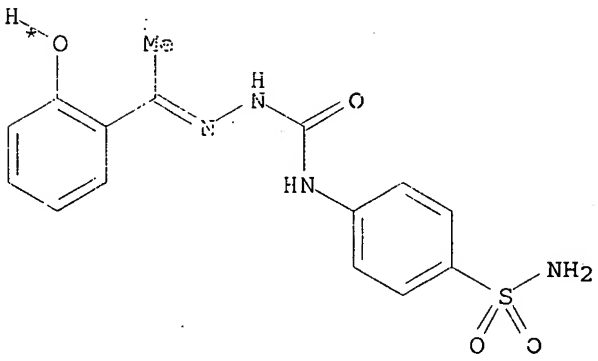
AB: CM 2

RX(14) RCT E 613221-32-2

STAGE(1)
RGT C 1310-65-2 LiOH
SOL 7732-18-5 Water, 64-17-5 EtOH

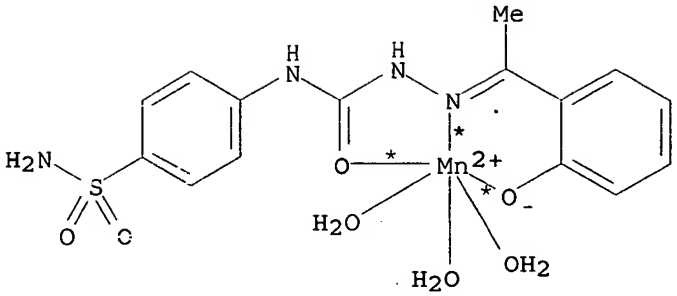
STAGE(2)
RGT X 7758-98-7 CuSO4
SOL 7732-18-5 Water
PRO AB 613221-49-1

RX(15) OF 79 ...G ===> AC



G

(15)



● $Cl^-$

● $H_2O$

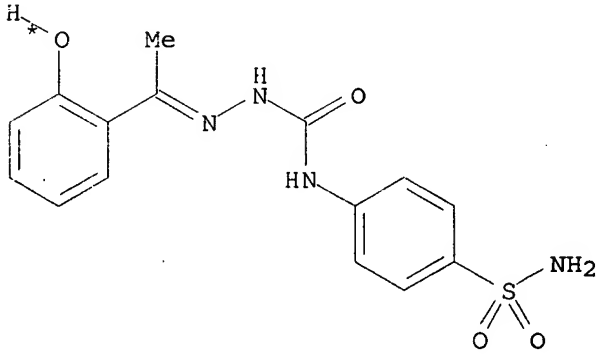
AC

RX(15) RCT G 613221-33-3

STAGE(1)
RGT O 1310-65-2 LiOH
SOL 7732-18-5 Water, 64-17-5 EtOH

STAGE(2)
RGT P 7773-01-5 MnCl2
SOL 7732-18-5 Water
PRO AC 613221-50-4

RX(16) OF 79 ...G + R ===> AD



G

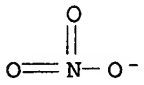
$H_3C-CH_2-OH$

R

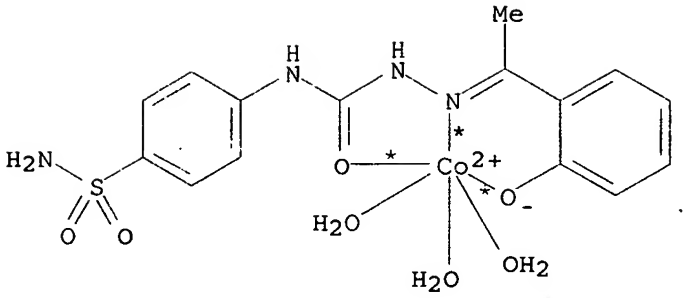
(16) ⟶

$H_3C-CH_2-OH$

AD: CM 1



AD: CM 2



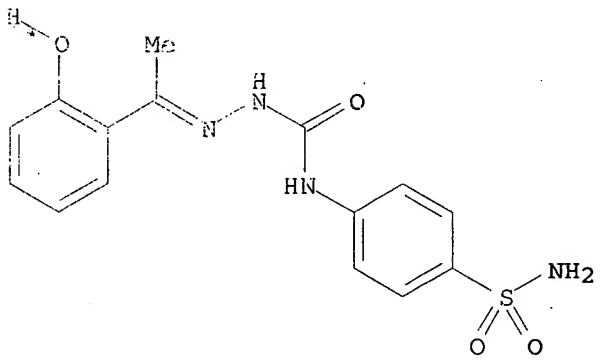
AD: CM 3

RX(16) RCT G 613221-33-3, R 64-17-5

STAGE(1)
RGT O 1310-65-2 LiOH
SOL 7732-18-5 Water, 64-17-5 EtOH

STAGE(2)
RGT T 10141-05-6 Co(NO3)2
SOL 7732-18-5 Water
PRO AD 613221-53-7

RX(17) OF 79 ...G ===> AE



G (17)

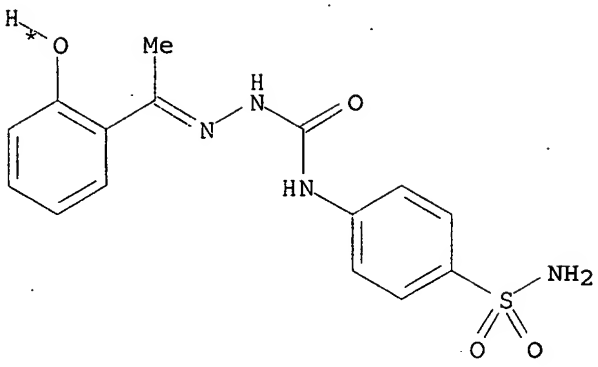
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(17) RCT G 613221-33-3

STAGE(1)
RGT O 1310-65-2 LiOH
SOL 7732-18-5 Water, 64-17-5 EtOH

STAGE(2)
RGT V 7718-54-9 NiCl2
SOL 7732-18-5 Water
PRO AE 613221-54-8

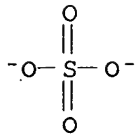
RX(18) OF 79 ...G + R ===> AF



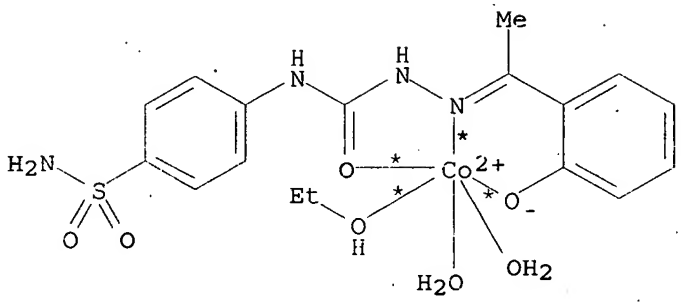
G

R

(18)



AF: CM 1



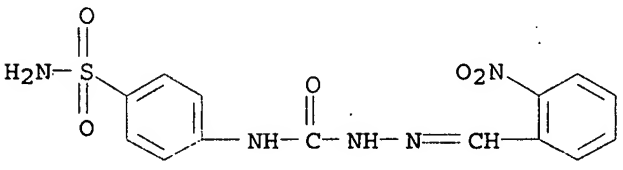
AF: CM 2

RX(18) RCT G 613221-33-3, R 64-17-5

STAGE(1)
RGT O 1310-65-2 LiOH
SOL 7732-18-5 Water, 64-17-5 EtOH

STAGE(2)
RGT X 7758-98-7 CuSO4
SOL 7732-18-5 Water
PRO AF 613221-56-0

RX(19) OF 79 ...I ===> AG



I

STRUCTURE DIAGRAM IS NOT AVAILABLE

(19)

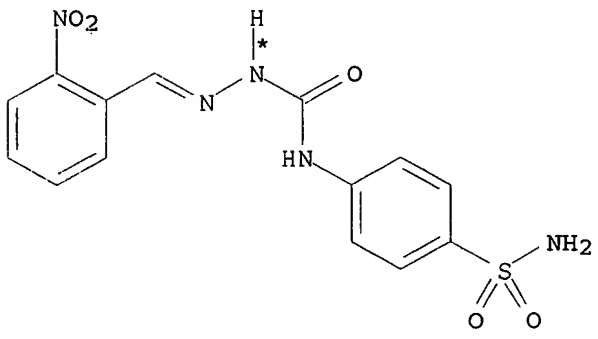
AG

RX(19) RCT I 613221-34-4

STAGE(1)
RGT O 1310-65-2 LiOH
SOL 7732-18-5 Water, 64-17-5 EtOH

STAGE(2)
RGT P 7773-01-5 MnCl2
SOL 7732-18-5 Water
PRO AG 613221-57-1

RX(20) OF 79 ...2 I ===> AH



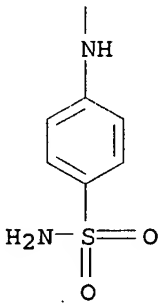
2 I

(20)



* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *





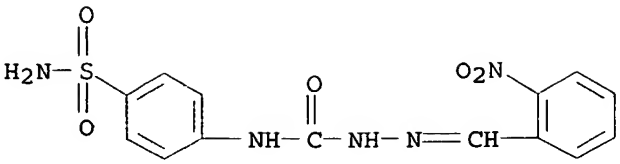
AH

RX(20) RCT I 613221-34-4

STAGE(1)
RGT O 1310-65-2 LiOH
SOL 7732-18-5 Water, 64-17-5 EtOH

STAGE(2)
RGT T 10141-05-6 Co(NO3)2
SOL 7732-18-5 Water
PRO AH 613221-58-2

RX(21) OF 79 ...I + 2 R ===> AI



$H_3C-CH_2-OH$

2 R

(21)

I

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *



● 2 $Cl^-$

● $H_2O$

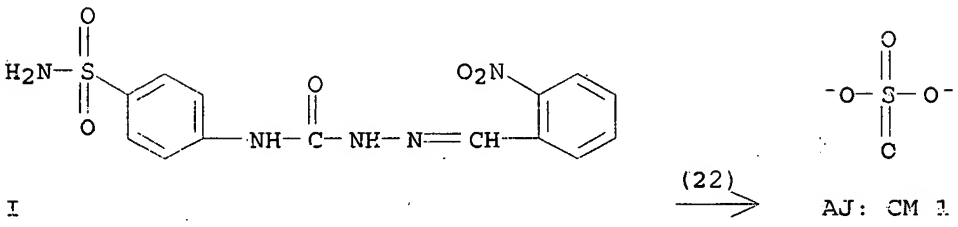
AI

RX(21) RCT I 613221-34-4, R 64-17-5

STAGE(1)
RGT O 1310-65-2 LiOH
SOL 7732-18-5 Water, 64-17-5 EtOH

STAGE(2)
RGT V 7718-54-9 NiCl2
SOL 7732-18-5 Water
PRO AI 613221-59-3

RX(22) OF 79 ...I ===> AJ



I

(22)

AJ: CM 1

STRUCTURE
DIAGRAM
IS NOT
AVAILABLE

AJ: CM 2

RX(22) RCT I 613221-34-4

STAGE(1)

RGT O 1310-65-2 LiOH
SOL 7732-18-5 Water, 64-17-5 EtOH

STAGE(2)
RGT X 7758-98-7 CuSO4
SOL 7732-18-5 Water
PRO AJ 613221-62-8

L4 ANSWER 3 OF 4 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 138:361747 CASREACT
TITLE: Synthesis and antimicrobial activity of copper-, cobalt- and nickel(II) complexes with Schiff bases
AUTHOR(S): Jadegoud, Y.; Ijare, Omkar B.; Mallikarjuna, N. N.; Angadi, S. D.; Mruthyunjayaswamy, B. H. M.
CORPORATE SOURCE: Department of Chemistry, Gulbarga University, Gulbarga, 585 106, India
SOURCE: Journal of the Indian Chemical Society (2002), 79(12), 921-924
CODEN: JICSAH; ISSN: 0019-4522
PUBLISHER: Indian Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 78-7 (Inorganic Chemicals and Reactions)
Section cross-reference(s): 1, 10, 28

ABSTRACT:
A few complexes of CuII, CoII and NiII were prepared by reacting their metal(II) chlorides with 3-(4'-phenylthiazole-2'-yl)-1-(2'-hydroxy-1'-iminomethylphenyl)urea and with 3-(4'-phenylthiazole-2'-yl)-1-(2',4'-dihydroxy/2'-hydroxy-5'-chloro-1'-methyliminomethylphenyl)ureas (Schiff bases) in EtOH medium. The chelates are colored solids and nonelectrolytes ML2. The IR spectra of the ligands and complexes suggest involvement of o-hydroxy group, carbonyl group, azomethine group in bonding through O and N atoms resp. The electronic spectra and magnetic data suggest the octahedral stereochem. for all the complexes in which metal(II) ion exhibits coordination number six. The ligands and complexes were tested for their antimicrobial activity.

SUPPL. TERM: **transition metal** salicylidenethiazolylurea complex prepn; salicylidenethiazolylurea prepn complexation **transition metal**; antibacterial activity **transition metal** salicylidenethiazolylurea complex; fungicidal activity **transition metal** salicylidenethiazolylurea complex

INDEX TERM: **Transition metal** complexes
ROLE: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(Schiff base; preparation and antibacterial and fungicidal activities)

INDEX TERM: Antibacterial agents
Fungicides
(preparation of **transition metal** salicylidenethiazolylurea complexes as)

INDEX TERM: Schiff bases
ROLE: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(**transition metal** complexes; preparation and antibacterial and fungicidal activities)

INDEX TERM: 519141-72-1P 519141-73-2P 519141-75-4P 519141-76-5P
ROLE: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antibacterial and fungicidal activities)

INDEX TERM: 519141-78-7P 519141-79-8P 519141-80-1P
ROLE: PAC (Pharmacological activity); RCT (Reactant); SPN

(Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation and complexation with **transition metals** and antibacterial and fungicidal activities)

INDEX TERM: 3673-36-7P 519141-81-2P, 4-Phenylthiazole-2-semicarbazide
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reactant for preparation of salicylidenethiazolylurea derivs.)

INDEX TERM: 519141-69-6P 519141-70-9P 519141-71-0P 519141-74-3P 519141-77-6P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

INDEX TERM: 89-84-9 90-02-8, Salicylaldehyde, reactions 122-51-0, Ethyl orthoformate 302-01-2, Hydrazine, reactions 1450-74-4 2010-06-2, 4-Phenyl-2-aminothiazole
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reactant for preparation of salicylidenethiazolylurea derivs.)

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S):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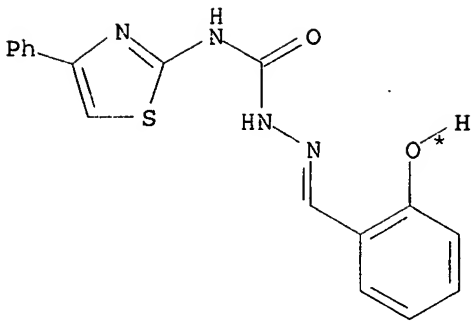
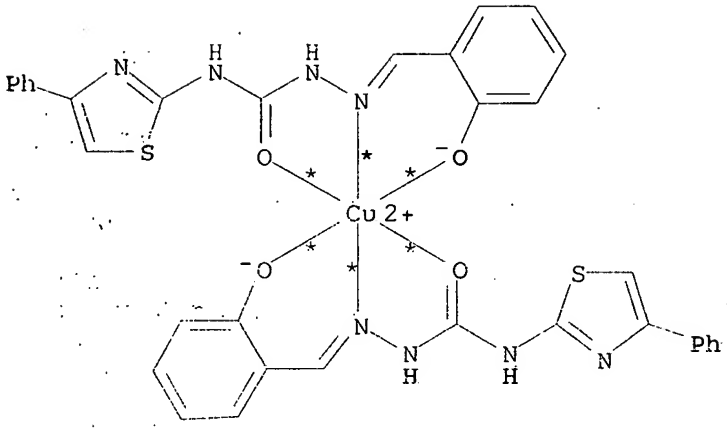


2 A

(1) →



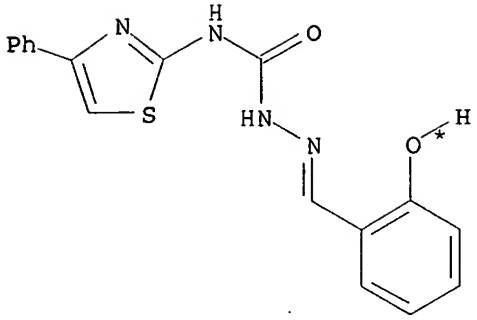
B
YIELD 88%

RX(1) RCT A 519141-78-7

STAGE(1)
RGT C 7447-39-4 CuCl2
SOL 64-17-5 EtOH

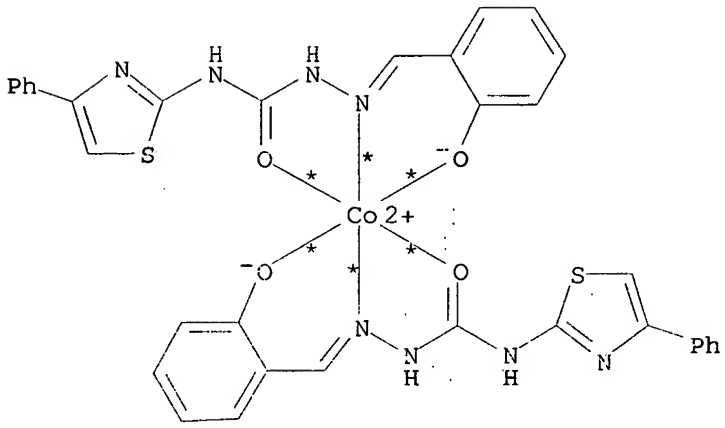
STAGE(2)
RGT D 127-09-3 AcONa
PRO B 519141-69-6

RX(2) OF 48 ...2 A ===> F



2 A

(2) →



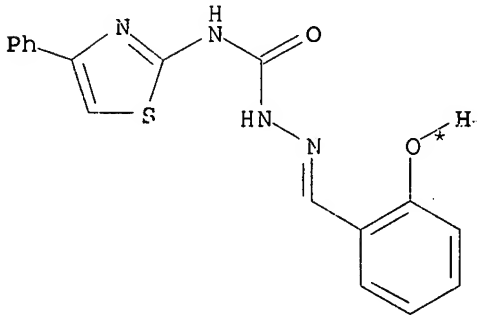
F
YIELD 89%

RX(2) RCT A 519141-78-7

STAGE(1)
RGT G 7646-79-9 CoCl2
SOL 64-17-5 EtOH

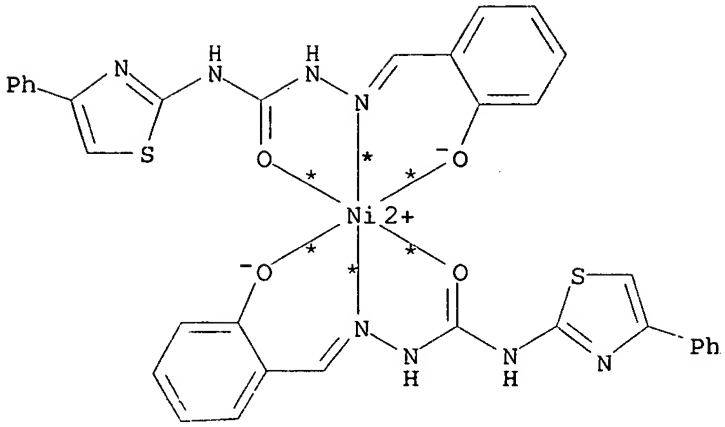
STAGE(2)
RGT D 127-09-3 AcONa
PRO F 519141-70-9

RX(3) OF 48 ...2 A ===> H



2 A

(3) →



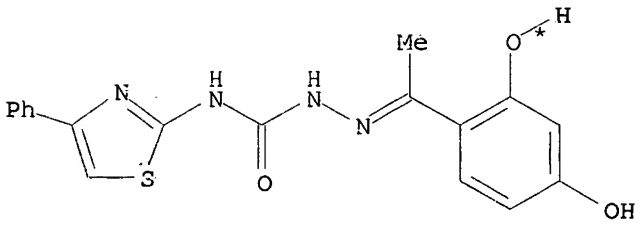
H
YIELD 88%

RX(3) RCT A 519141-78-7

STAGE(1)
RGT I 7718-54-9 NiCl2
SOL 64-17-5 EtOH

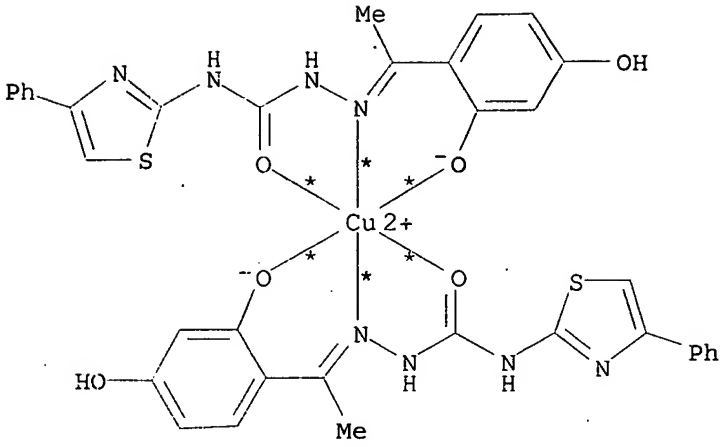
STAGE(2)
RGT D 127-09-3 AcONa
PRO H 519141-71-0

RX(4) OF 48 ...2 J ===> K



2 J

(4) →



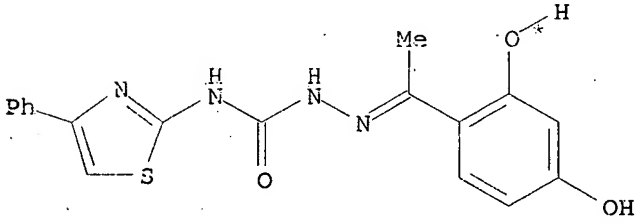
K
YIELD 98%

RX(4) RCT J 519141-79-8

STAGE(1)
RGT C 7447-39-4 CuCl2
SOL 64-17-5 EtOH

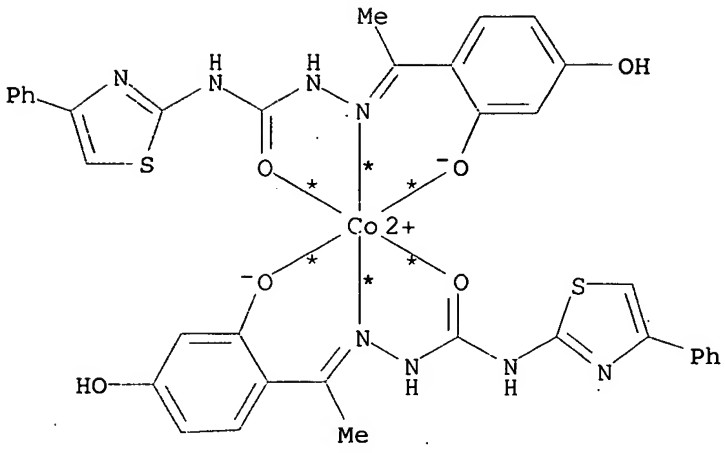
STAGE(2)
RGT D 127-09-3 AcONa
PRO K 519141-72-1

RX(5) OF 43 ...2 J ===> L



2 J

(5)



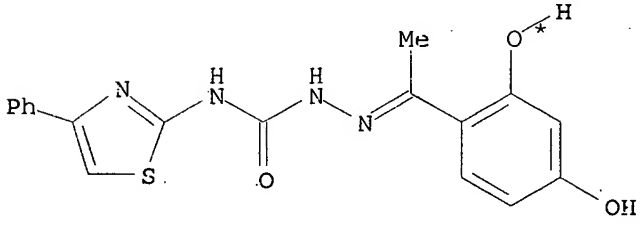
L
YIELD 88%

RX(5) RCT J 519141-79-8

STAGE(1)
RGT G 7646-79-9 CoCl2
SOL 64-17-5 EtOH

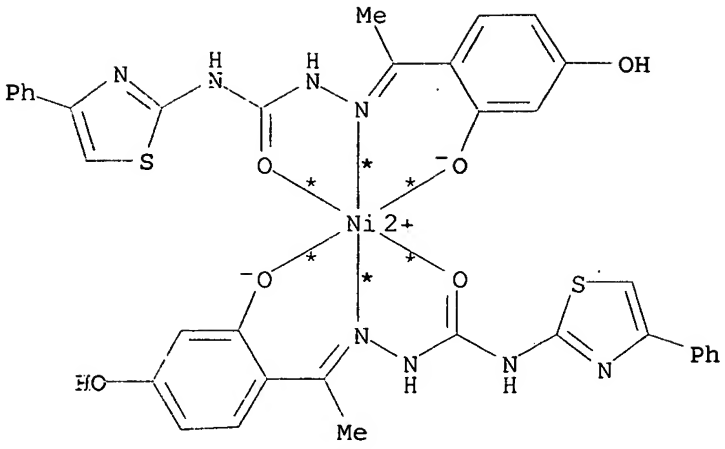
STAGE(2)
RGT D 127-09-3 AcONa
PRO L 519141-73-2

RX(6) OF 46 ...2 J ===> M



2 J

(6) ⟶



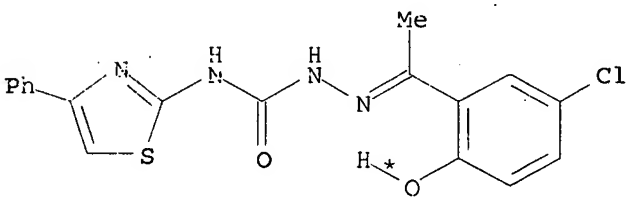

M
YIELD 88%

RX(6) RCT J 519141-79-8

STAGE(1)
RGT I 7718-54-9 NiCl2
SOL 64-17-5 EtOH

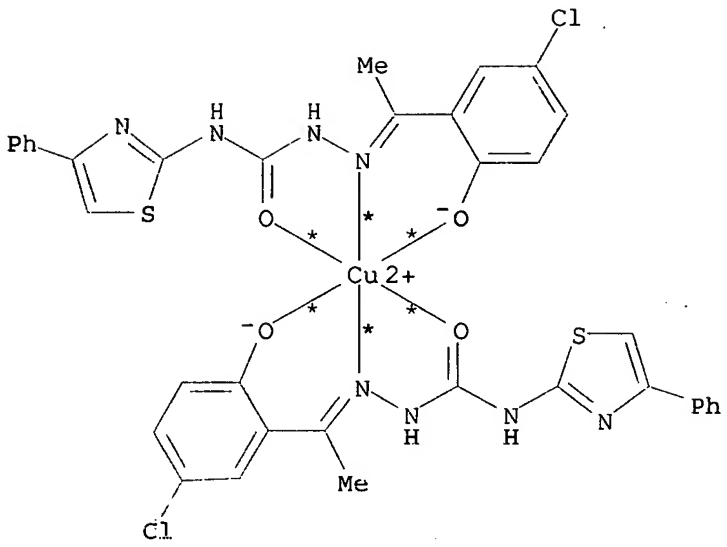
STAGE(2)
RGT D 127-09-3 AcONa
PRO M 519141-74-3

RX(7) OF 43 ...2 N ===> O




2 N

(7) →



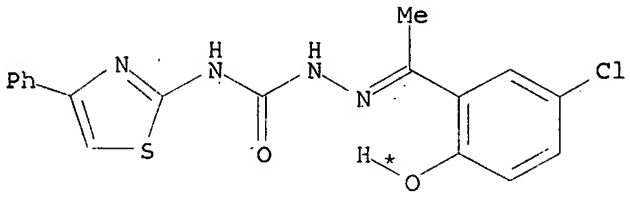
O
YIELD 88%

RX(7) RCT N 519141-80-1

STAGE(1)
RGT C 7447-39-4 CuCl2
SOL 64-17-5 EtOH

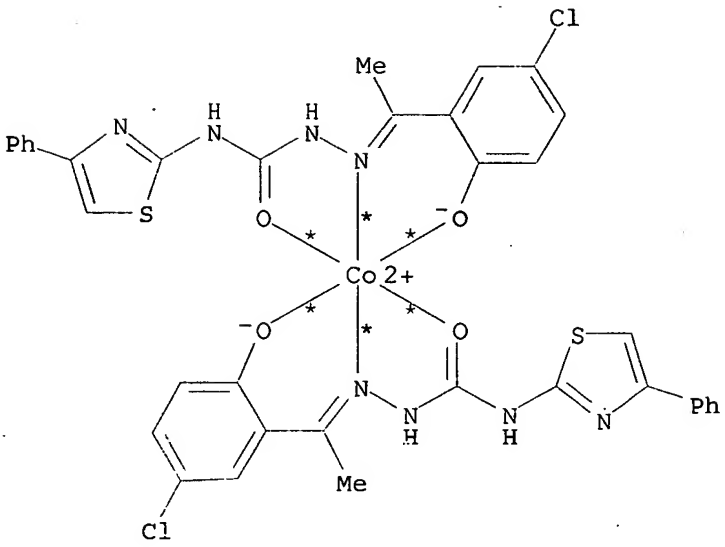
STAGE(2)
RGT D 127-09-3 AcONa
PRO O 519141-75-4

RX(8) OF 43 ...2 N ===> P



2 N

(8) →



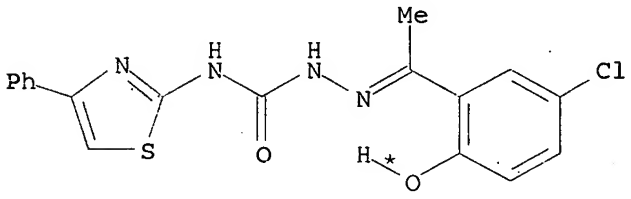
P
YIELD 88%

RX(8) RCT N 519141-80-1

STAGE(1)
RGT G 7646-79-9 CoCl2
SOL 64-17-5 EtOH

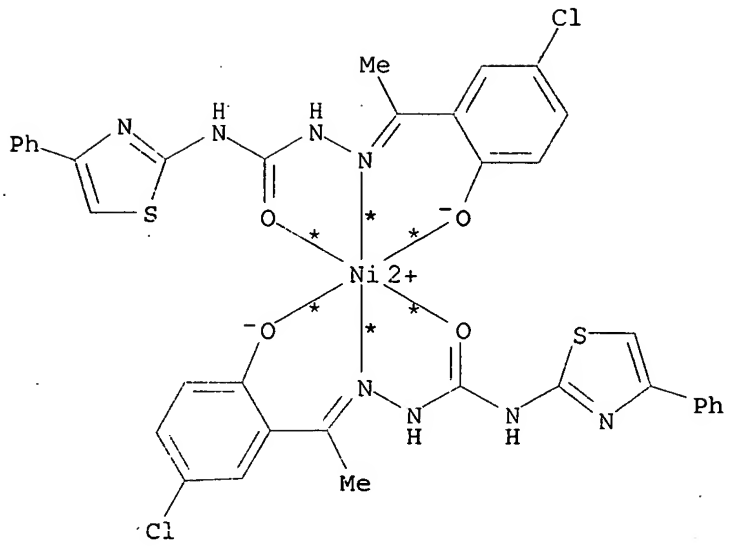
STAGE(2)
RGT D 127-09-3 AcONa
PRO P 519141-76-5

RX(9) OF 48 ...2 N ===> Q



2 N

(9) →



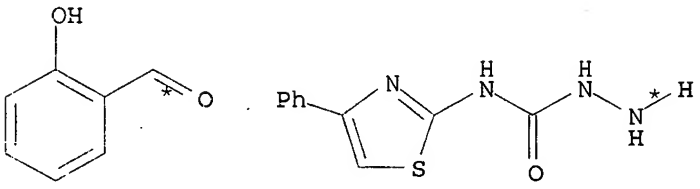
Q
YIELD 88%

RX(9) RCT N 519141-80-1

STAGE(1)
RGT I 7718-54-9 NiCl2
SOL 64-17-5 EtOH

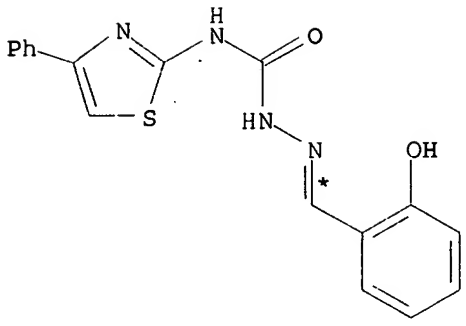
STAGE(2)
RGT D 127-09-3 AcONa
PRO Q 519141-77-6

RX(10) OF 48 ...R + S ===> A...



R S

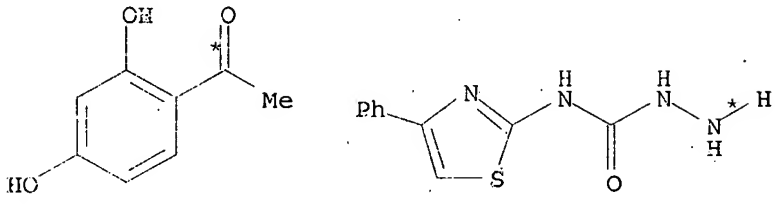
(10) ⟶



A
YIELD 94%

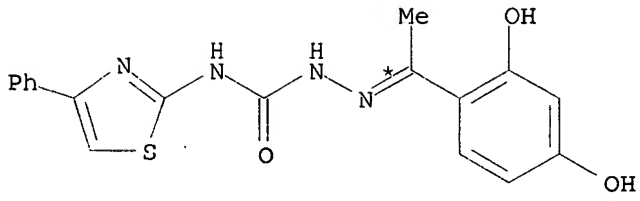
RX(10) RCT R 90-02-8, S 519141-81-2
PRO A 519141-78-7
CAT 7647-01-0 HCl
SOL 64-17-5 EtOH

RX(11) OF 48 ...U + S ===> J...



U S

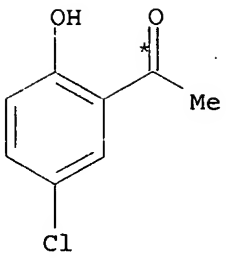
(11)

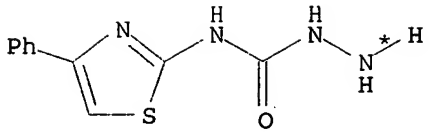


J
YIELD 60%

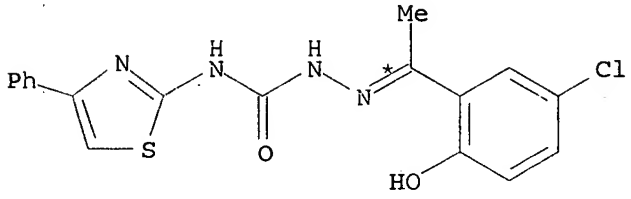
RX(11) RCT U 89-84-9, S 519141-81-2
PRO J 519141-79-8
CAT 7647-01-0 HCl
SOL 64-17-5 EtOH

RX(12) OF 48 ...V + S ===> N...





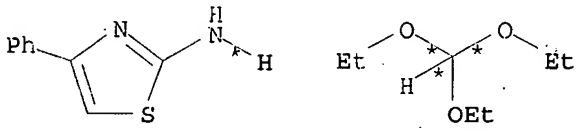
V S (12)



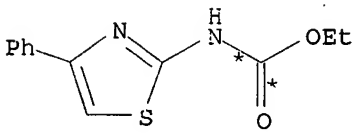
N
YIELD 90%

RX(12) RCT V 1450-74-4, S 519141-81-2
PRO N 519141-80-1
CAT 7647-01-0 HCl
SOL 64-17-5 EtOH

RX(13) OF 48 W + X ===> Y...



W X (13)



Y
YIELD 44%

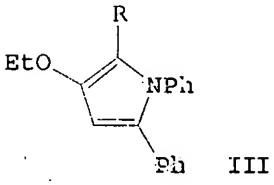
RX(13) RCT W 2010-06-2, X 122-51-0
PRO Y 3673-36-7
SOL 110-86-1 Pyridine

RX(14) OF 48 ...Y ===> S...

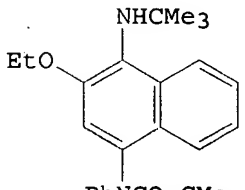
Y (14) S
YIELD 48%

RX(14) RCT Y 3673-36-7
RGT AA 302-01-2 N2H4
PRO S 519141-81-2
SOL 64-17-5 EtOH

L4 ANSWER 4 OF 4 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 121:108417 CASREACT
TITLE: Organic syntheses via **transition metal** complexes. 69. 2-(Acylamino)ethenyl ketene imines from [2-(acylamino)ethenyl]carbene complexes and their ring-closing metathesis to pyrroles or electrocyclization to 1,4-diaminonaphthalenes
AUTHOR(S): Aumann, Rudolf; Jasper, Beate; Goddard, Richard; Krueger, Carl
CORPORATE SOURCE: Org.-Chem. Inst., Univ. Muenster, Muenster, D-48149, Germany
SOURCE: Chemische Berichte (1994), 127(4), 717-24
CODEN: CHBEAM; ISSN: 0009-2940
DOCUMENT TYPE: Journal
LANGUAGE: German
CLASSIFICATION: 27-10 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 29
GRAPHIC IMAGE:



III



IV

ABSTRACT:
[2-(Acylamino)ethenyl]carbene complexes (CO)5M:C(OEt)CH:CPhNPhCOR [I, M = Cr, W; R = Ph, p-MeOC6H4, p-NO2C6H4, OCMe3] are obtained by N-acylation of (CO)5M:C(OEt)CH:CPhNHPh in 72-90% chemical yields with high stereoselectivity. The reaction of (Z)- or (E)-I with two equivalent of R1NC (R1 = cyclohexyl, CMe3) at 20° gives (CO)5M(RNC) and R1N:C:C(OEt)CH:CPhNPhCOR (II, >95% yields) with configurational retention at the C:C(N) bond. Thermolysis of (Z)-II (20-80°C) provides an efficient route to pyrroles III (90-95%) by a ring-closing metathesis with elimination of R1NCO, while the thermolysis of (E)-II (R = R1 = CMe3) at 20°C leads to the 1,4-diaminonaphthalene IV (>95% yield), by an electrocyclic ring closure.

SUPPL. TERM: acylaminoethenylcarbene complex prepn isocyanide reaction; acylaminoethenylketenimine prepn thermolysis; pyrrole diaryl; naphthalenediamine

INDEX TERM: Double decomposition
(of acylaminoethenylketenimines, pyrroles by)

INDEX TERM: Ring closure and formation
(electrocyclic, of acylaminoethenylketenimines)

INDEX TERM: 155804-99-2P 155805-01-9P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of acylaminoethenylketenimines)

INDEX TERM: 155700-54-2P 155700-55-3P 155700-56-4P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and thermolysis of)

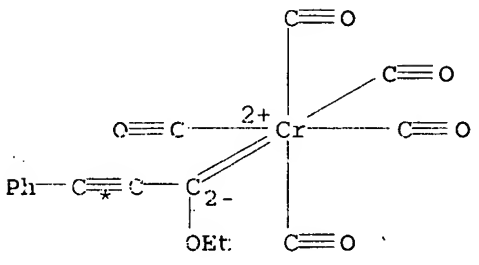
INDEX TERM: 62465-44-5P 155700-57-5P 155700-58-6P 155700-59-7P 155700-60-0P 155700-61-1P 155700-62-2P 155700-63-3P 155805-00-8P 155805-02-0P 155897-38-4P 155897-39-5P 156856-16-5P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

INDEX TERM: 155804-98-1P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(preparation, crystal structure and reaction of, in preparation of acylaminoethenylketenimines)

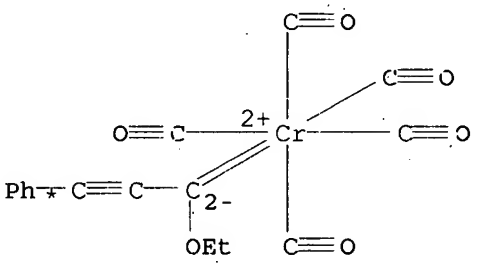
INDEX TERM: 98-88-4, Benzoyl chloride 100-07-2, 4-Methoxybenzoyl chloride 122-04-3, 4-Nitrobenzoyl chloride 34619-03-9, Di-tert-butyl carbonate 36009-07-1 153452-50-7
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of acylaminoethenylketenimines)

INDEX TERM: 931-53-3, Cyclohexyl isocyanide 7188-38-7, tert-Butyl isocyanide
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with acylaminoethenylketenimines)

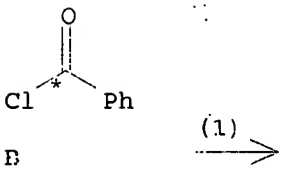
RX(1) OF 6 2 A + B ===> C...



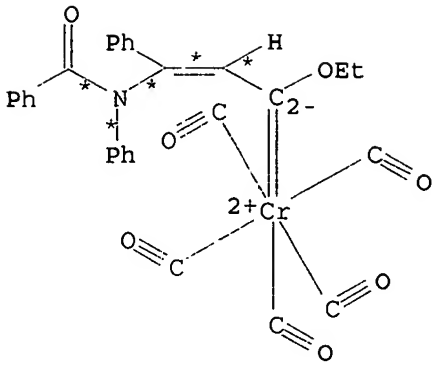
A



A



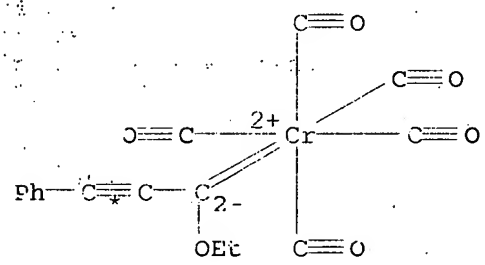
B



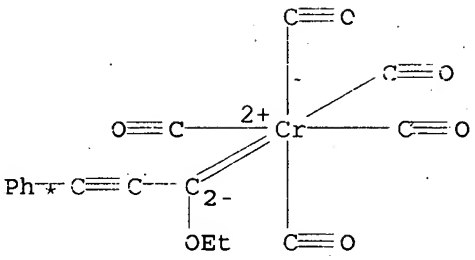
C
YIELD 80%

RX(1) RCT A 36009-07-1, B 98-88-4
RGT D 121-44-8 Et3N
PRO C 155804-98-1
CAT 1122-58-3 4-DMAP
SOL 75-09-2 CH2Cl2, 60-29-7 Et2O

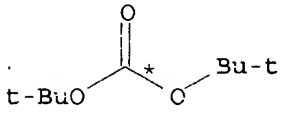
RX(2) OF 6 2 A + H ===> I...



A

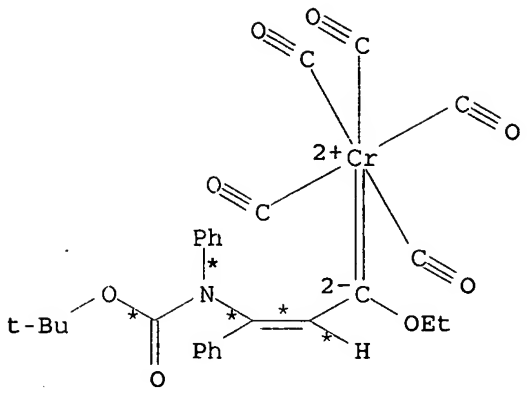


A



H

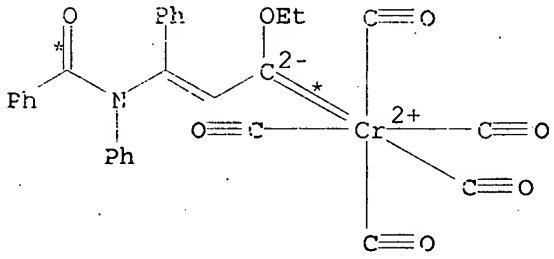
(2) ⟶



I
YIELD 80%

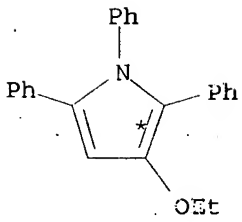
RX(2) RCT A 36009-07-1, H 34619-03-9
PRO I 155897-39-5
CAT 1122-58-3 4-DMAP
SOL 109-99-9 THF

RX(3) OF 6 ...C ===> K



C

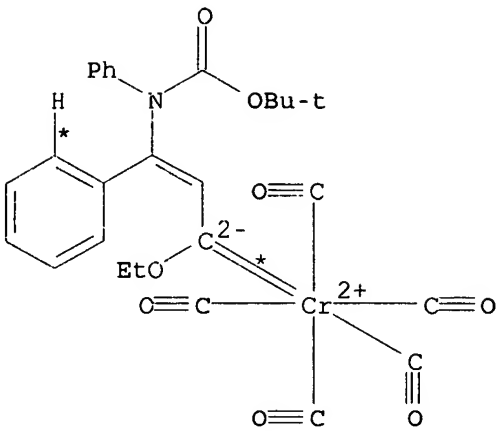
(3) ⟶



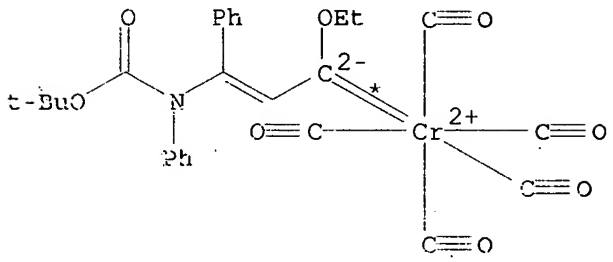
K
YIELD 95%

RX(3) RCT C 155804-98-1
RGT L 931-53-3 C6H11NC
PRO K 155700-50-0
NTE ligroin solvent

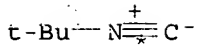
RX(4) OF 6 ...2 I + 2 M ===> N + O



I

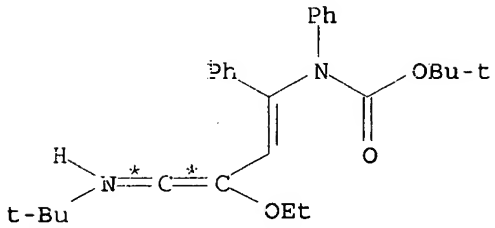


J

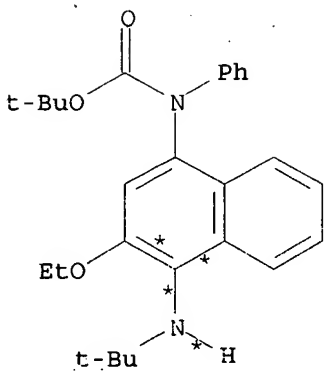


2 M

(4)



N



O

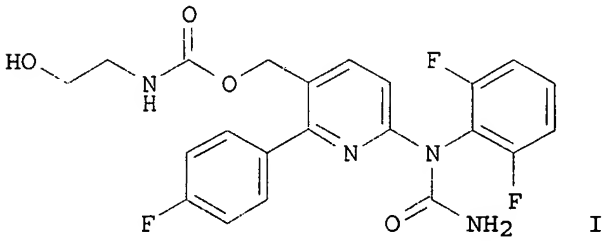
RX(4) RCT I **155897-39-5**, M 7188-38-7
PRO N 155700-62-2, O **155700-63-3**
SOL 60-29-7 Et2O

4/14/05

ANSWER 2 OF 150 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 141:225319 CASREACT
TITLE: Process for preparation of N-heteroaryl-N-aryl-amines
INVENTOR(S): Snoonian, John R.; Oliver-Shaffer, Patrica-Ann
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C07D213-80
SECONDARY: C07D213-79; C07D213-75; C07C273-18; C07C275-42; C07C275-30
CLASSIFICATION: 27-16 (Heterocyclic Compounds (One Hetero Atom))
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004072038 | A1 | 20040826 | WO 2004-US3933 | 20040210 |
| W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2004230058 | A1 | 20041118 | US 2004-775687 | 20040210 |
| PRIORITY APPLN. INFO.: | | | US 2003-446641P | 20030210 |
| | | | US 2003-474272P | 20030528 |

OTHER SOURCE(S): MARPAT 141:225319
GRAPHIC IMAGE:



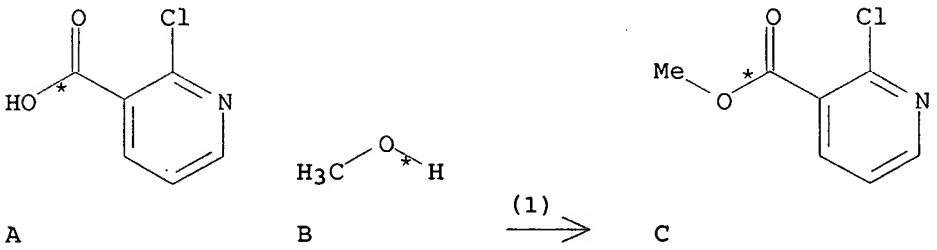
I

ABSTRACT:
The present invention relates to a process for producing diarylamine derivs. with general formula of Ar1-NH-Ar2 [wherein Ar1 and Ar2 = independently (un)substituted aryl or heteroaryl] or salts thereof, which comprises coupling a compound of formula Ar1-X [where X = a leaving group] with an amine of formula Ar2-NH-Y [where Y = CO2Z; Z = alkyl, PhCH2, Fmoc, etc.] in the presence of an alkali metal salt or a transition metal catalyst. For example, the compound I was prepared starting from 6-chloro-2-(4-fluorophenyl)nicotinic acid Me ester (preparation given) and N-(tert-butoxycarbonyl)-2,6-difluoroaniline.

SUPPL. TERM: prepn hetero aryl amine coupling reaction catalyst base
INDEX TERM: Amines, preparation
ROLE: IMF (Industrial manufacture); SPN (Synthetic

preparation); PREP (Preparation)
(diamines, aromatic; preparation of
N-heteroaryl-N-aryl-amines)
INDEX TERM: Coupling reaction
(preparation of N-heteroaryl-N-aryl-amines)
INDEX TERM: Transition metals, uses
ROLE: CAT (Catalyst use); USES (Uses)
(preparation of N-heteroaryl-N-aryl-amines)
INDEX TERM: Alkali metal salts
ROLE: RGT (Reagent); RACT (Reactant or reagent)
(preparation of N-heteroaryl-N-aryl-amines)
INDEX TERM: Bases, reactions
ROLE: RGT (Reagent); RACT (Reactant or reagent)
(preparation of N-heteroaryl-N-aryl-amines)
INDEX TERM: Coupling reaction catalysts
(transition metals; preparation of N-heteroaryl-N-aryl-amines)
INDEX TERM: 40134-18-7P 210161-08-3P 223760-99-4P 250123-28-5P
745833-06-1P 745833-08-3P 745833-10-7P 745833-21-0P
ROLE: IMF (Industrial manufacture); RCT (Reactant); SPN
(Synthetic preparation); PREP (Preparation); RACT (Reactant
or reagent)
(intermediate; preparation of N-heteroaryl-N-aryl-amines)
INDEX TERM: 7440-05-3, Palladium, uses
ROLE: CAT (Catalyst use); USES (Uses)
(preparation of N-heteroaryl-N-aryl-amines)
INDEX TERM: 745833-13-0P 745833-15-2P 745833-23-2P
ROLE: IMF (Industrial manufacture); SPN (Synthetic
preparation); PREP (Preparation)
(preparation of N-heteroaryl-N-aryl-amines)
INDEX TERM: 503-38-8, Diphosgene 1336-21-6, Ammonium hydroxide
1765-93-1, 4-Fluorophenylboronic acid 2942-59-8,
2-Chloronicotinic acid 745833-17-4 745833-19-6
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(preparation of N-heteroaryl-N-aryl-amines)
INDEX TERM: 497-19-8, Sodium carbonate, reactions 534-17-8, Cesium
carbonate 584-08-7, Potassium carbonate 865-47-4
865-48-5 1310-73-2, Sodium hydroxide, reactions
7440-09-7D, Potassium, salts 7440-17-7D, Rubidium, salts
7440-46-2D, Cesium, salts 7647-01-0, Hydrogen chloride,
reactions 7778-53-2, Potassium phosphate
ROLE: RGT (Reagent); RACT (Reactant or reagent)
(preparation of N-heteroaryl-N-aryl-amines)

RX(1) OF 37 A + B ===> C...



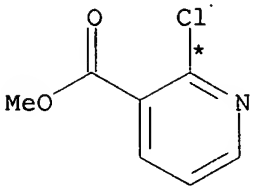

A B C

RX(1) RCT A 2942-59-8

STAGE(1)
RGT D 7719-09-7 SOCl2
SOL 75-09-2 CH2Cl2

STAGE(2)
RCT B 67-56-1
PRO C 40134-18-7

RX(2) OF 37 ...C + F ===> G...



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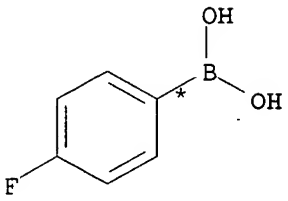

F

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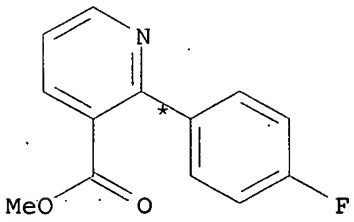
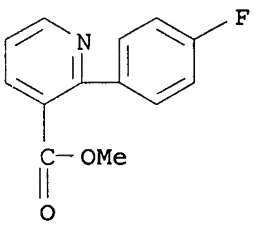


G

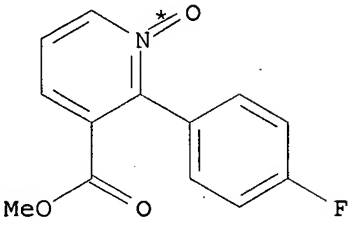
RX(2) RCT C 40134-18-7, F 1765-93-1
RGT H 497-19-8 Na2CO3
PRO G 210161-08-3
CAT 14221-01-3 Pd(PPh3)4
SOL 64-17-5 EtOH

RX(3) OF 37 ...G ===> K...



G

(3) →



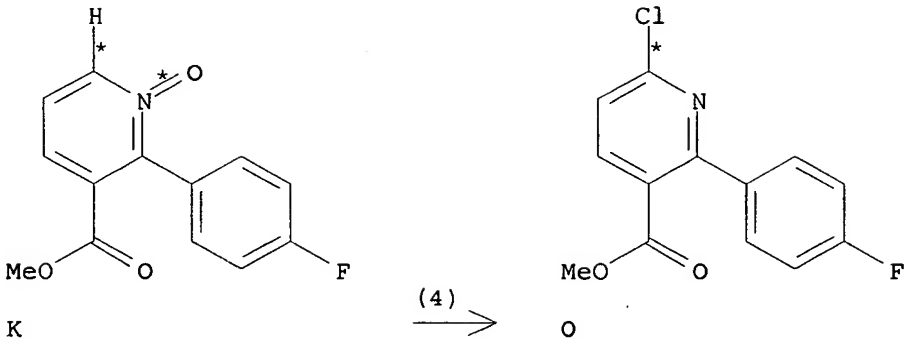
K

RX(3) RCT G 210161-08-3

STAGE(1)
RGT L 124-43-6 Urea-H2O2, M 64-19-7 AcOH
SOL 7732-18-5 Water

STAGE(2)
SOL 7732-18-5 Water
PRO K 223760-99-4
NTE workup

RX(4) OF 37 ...K ===> O...



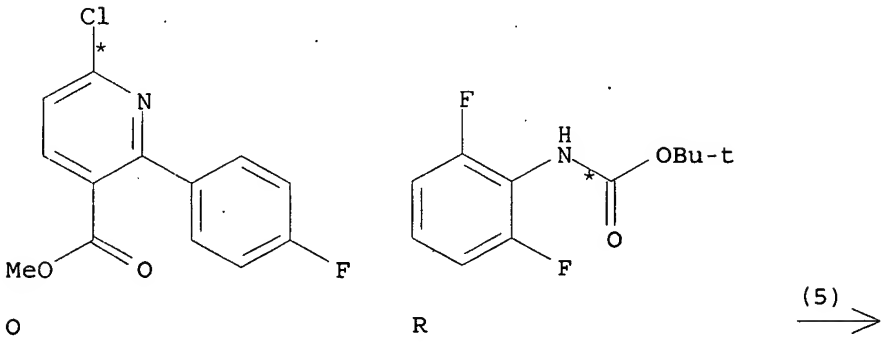

K O

RX(4) RCT K 223760-99-4

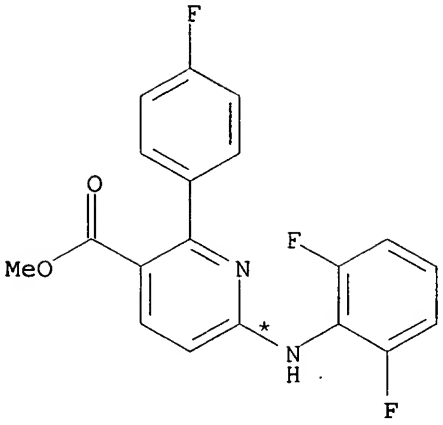
STAGE(1)
RGT P 10025-87-3 POCl3
SOL 107-06-2 ClCH2CH2Cl

STAGE(2)
RGT N 7732-18-5 Water
PRO O 745833-06-1

RX(5) OF 37 ...O + R ===> S...




O R



S

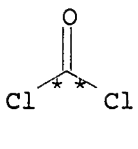
RX(5)

STAGE(1)
RGT T 98327-87-8 Phosphine, [1,1'-binaphthalene]-2,2'-diylbis[diphenyl-
CAT 3375-31-3 Pd(OAc)2
SOL 108-88-3 PhMe

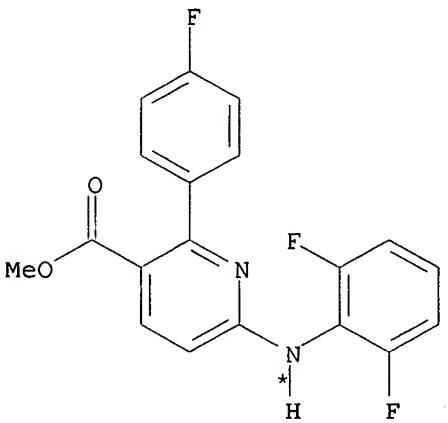
STAGE(2)
RCT O **745833-06-1**, R **745833-17-4**
RGT U 7778-53-2 K3PO4

STAGE(3)
RGT V 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2
PRO S **745833-08-3**
NTE workup

RX(6) OF 37 ...Y + S ===> Z...

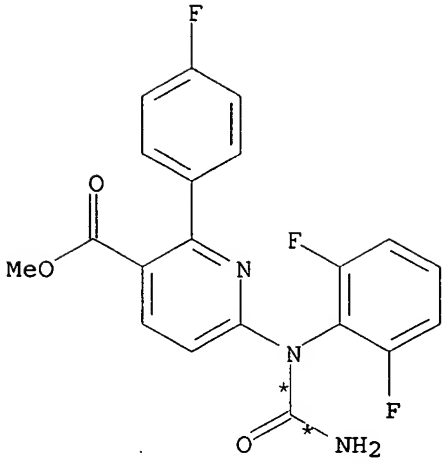


Y



S

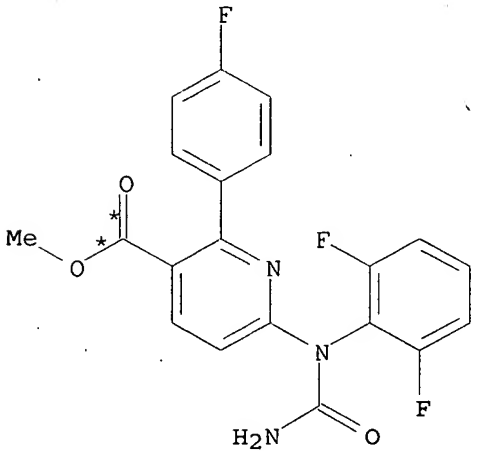
(6) →



Z

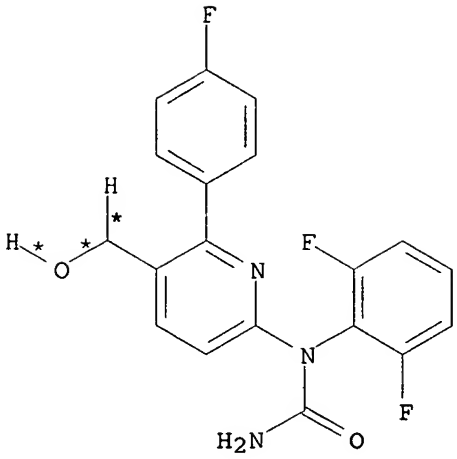
RX(6) RCT Y 75-44-5, S 745833-08-3
RGT AA 7727-37-9 N2
PRO Z 745833-10-7
SOL 108-88-3 PhMe

RX(7) OF 37 ...Z ===> AB...



Z

(7) →



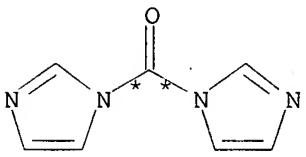
AB
YIELD 80%

RX(7) RCT Z 745833-10-7

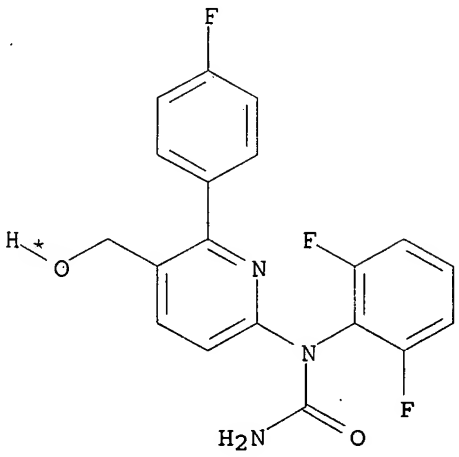
STAGE(1)
RGT AC 1191-15-7 AlH(Bu-i)2
SOL 109-99-9 THF

STAGE(2)
RGT AD 7664-93-9 H2SO4
SOL 7732-18-5 Water
PRO AB 250123-28-5

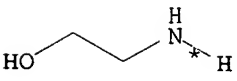
RX(8) OF 37 ...AF + AB + AG ===> AH



AF

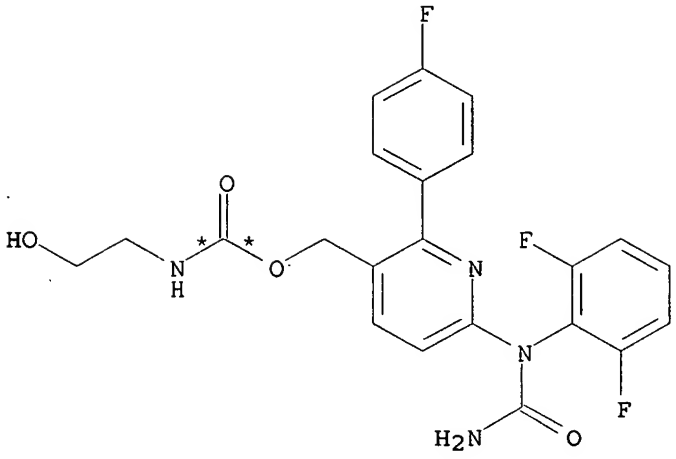


AB



AG

(8) ⟶



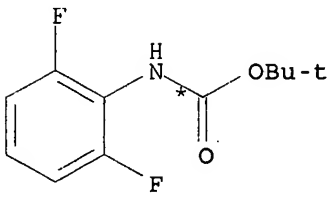
AH

RX(8) RCT AF 530-62-1, AB 250123-28-5

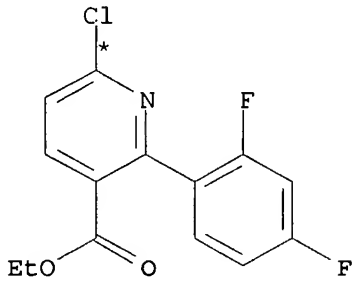
STAGE(1)
SOL 109-99-9 THF

STAGE(2)
RCT AG 141-43-5
SOL 75-05-8 MeCN
PRO AH 745833-13-0

RX(9) OF 37 **R + AJ ===> AK**

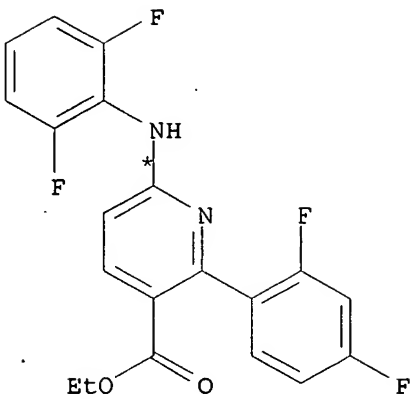


R



AJ

(9) ⟶



● HCl

AK
YIELD 71%

RX(9) RCT R **745833-17-4**, AJ **745833-19-6**

STAGE(1)
RGT AL 534-17-8 Cs2CO3
SOL 872-50-4 NMEP

STAGE(2)
SOL 7732-18-5 Water

STAGE(3)
RGT V 76-05-1 F3CCO2H
SOL 7732-18-5 Water
PRO AK **745833-15-2**

L2 ANSWER 4 OF 150 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 141:190989 CASREACT
TITLE: Facile synthesis of acyclic azanucleosides from N-pivaloyloxymethyl amides and sulfonamides: synthesis of aza-analogues of Ganciclovir
AUTHOR(S): Koszytkowska-Stawinska, Mariola; Sas, Wojciech
CORPORATE SOURCE: Faculty of Chemistry, Warsaw University of Technology, Warsaw, 00-664, Pol.
SOURCE: Tetrahedron Letters (2004), 45(28), 5437-5440
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 33-9 (Carbohydrates)
ABSTRACT:
N-Pivaloyloxymethyl amides and sulfonamides, readily available from N-alkylation of both amides and sulfonamides with com. chloromethyl pivaloate, were converted into acyclic azanucleosides via a one-pot base silylation/nucleoside coupling procedure.

SUPPL. TERM: acyclic azanucleoside prepn; pivaloyloxymethyl amide sulfonamide silylation nucleoside coupling
INDEX TERM: Coupling reaction
(nucleoside; synthesis of acyclic azanucleosides from N-pivaloyloxymethyl amides and sulfonamides via one-pot

base silylation/nucleoside coupling)

INDEX TERM: Alkylation
Silylation
(synthesis of acyclic azanucleosides from N-pivaloyloxymethyl amides and sulfonamides via one-pot base silylation/nucleoside coupling)

INDEX TERM: Acyclonucleosides
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of acyclic azanucleosides from N-pivaloyloxymethyl amides and sulfonamides via one-pot base silylation/nucleoside coupling)

INDEX TERM: 82410-32-0P, Ganciclovir
ROLE: PNU (Preparation, unclassified); PREP (Preparation)
(synthesis of acyclic azanucleosides from N-pivaloyloxymethyl amides and sulfonamides via one-pot base silylation/nucleoside coupling)

INDEX TERM: 65-71-4 66-22-8, 2,4(1H,3H)-Pyrimidinedione, reactions
1124-53-4 18997-19-8 19299-40-2 26661-13-2
82919-04-8 112233-74-6 125482-58-8
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of acyclic azanucleosides from N-pivaloyloxymethyl amides and sulfonamides via one-pot base silylation/nucleoside coupling)

INDEX TERM: 90950-23-5P, 1,5-Dioxaspiro[5.5]undecan-3-amine
740801-28-9P 740801-29-0P 740801-33-6P 740801-34-7P
740801-35-8P 740801-36-9P 740801-37-0P 740801-43-8P
740801-44-9P 740801-47-2P 740801-48-3P 740801-49-4P
740801-50-7P 740801-52-9P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of acyclic azanucleosides from N-pivaloyloxymethyl amides and sulfonamides via one-pot base silylation/nucleoside coupling)

INDEX TERM: 740801-30-3P 740801-31-4P 740801-32-5P 740801-38-1P
740801-39-2P 740801-40-5P 740801-41-6P 740801-42-7P
740801-45-0P 740801-46-1P 740801-51-8P 740801-53-0P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of acyclic azanucleosides from N-pivaloyloxymethyl amides and sulfonamides via one-pot base silylation/nucleoside coupling)

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD.

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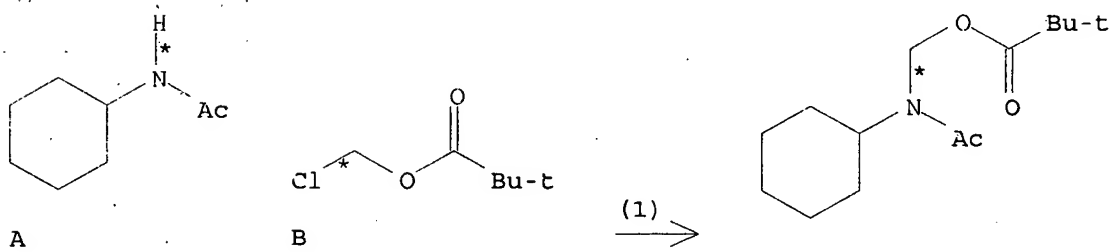
RX(1) OF 82 A + B ===> C...

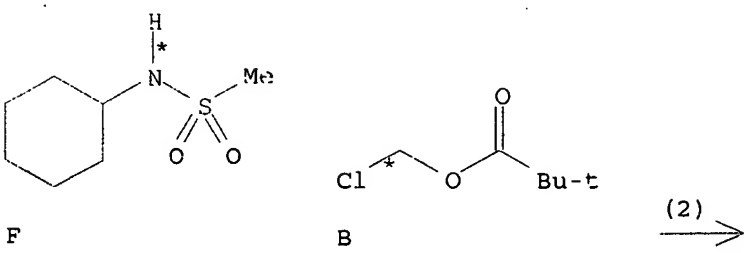



A B C

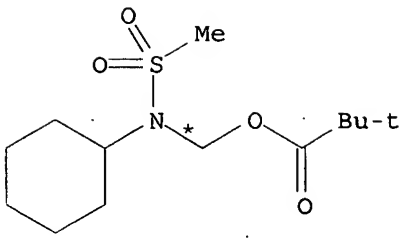
YIELD 50%

RX(1) RCT A 1124-53-4, B 18997-19-8
RGT D 7646-69-7 NaH
PRO C 740801-28-9
SOL 68-12-2 DMF

RX(2) OF 82 F + B ===> G...



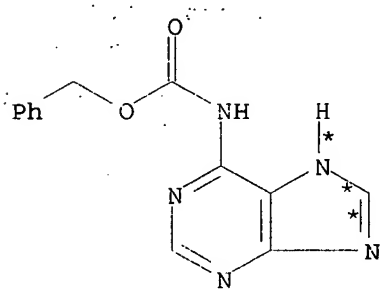

F B



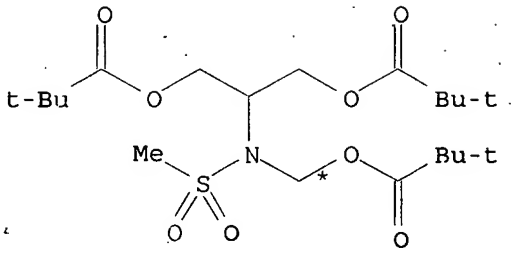
G
YIELD 72%

RX(2) RCT F 19299-40-2, B 18997-19-8
RGT D 7646-69-7 NaH
PRO G 740801-29-0
SOL 68-12-2 DMF

RX(3) OF 82 ...H + I ===> J...

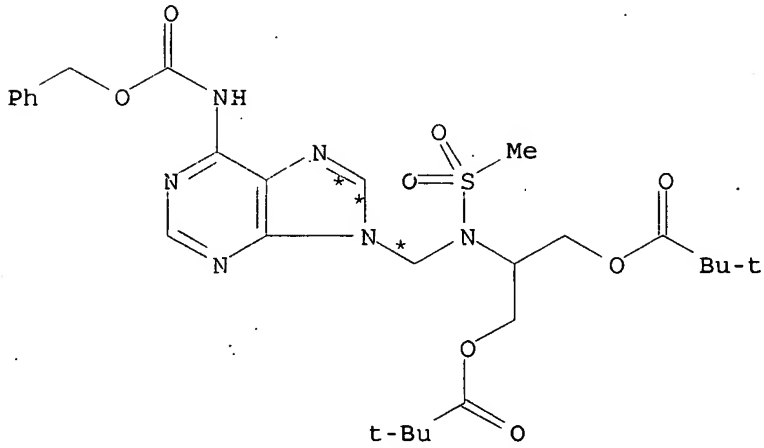


H



I

(3) →

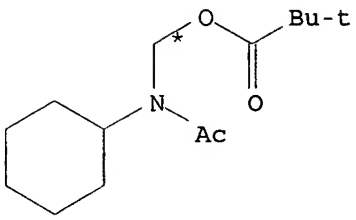


J
YIELD 44%

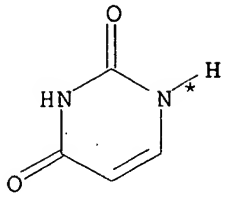
RX(3) RCT H 82919-04-8, I 740801-49-4
RGT K 10416-59-8 Me3SiN:CMeOSiMe3, L 7646-78-8 SnCl4
PRO J 740801-52-9

SOL 75-05-8 MeCN

RX(4) OF 82 ...C + N ===> O

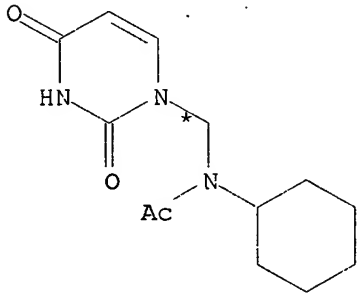


C



N

(4) →



O

YIELD 51%

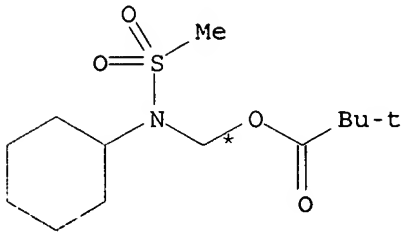
RX(4) RCT C 740801-28-9, N 66-22-8

STAGE(1)
RGT K 10416-59-8 Me3SiN:CMeOSiMe3
SOL 75-05-8 MeCN

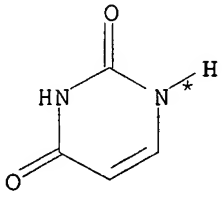
STAGE(2)
CAT 27607-77-8 Me3SiSO3CF3

PRO O 740801-30-3

RX(5) OF 82 ...G + N ===> Q

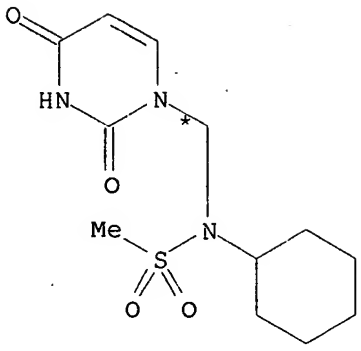


G'



N

(5) →



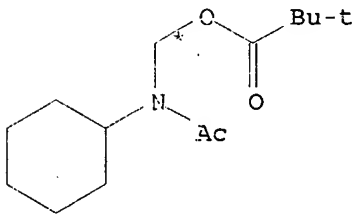
Q
YIELD 41%

RX(5) RCT G 740801-29-0, N 66-22-8

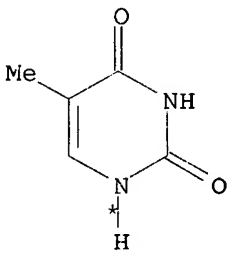
STAGE(1)
RGT K 10416-59-8 Me3SiN:CMeOSiMe3
SOL 75-05-8 MeCN

STAGE(2)
CAT 27607-77-8 Me3SiSO3CF3
PRO Q 740801-31-4

RX(6) OF 82 ...C + R ===> S

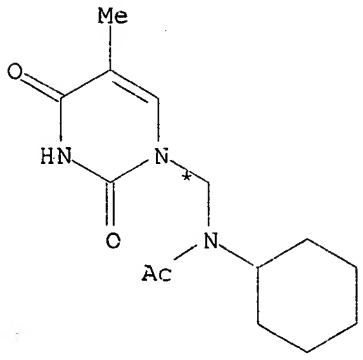


C



R

(6)



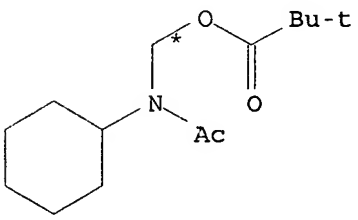
S
YIELD 70%

RX(6) RCT C 740801-28-9, R 65-71-4

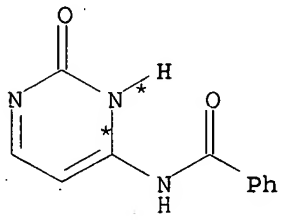
STAGE(1)
RGT K 10416-59-8 Me3SiN:CMeOSiMe3
SOL 75-05-8 MeCN

STAGE(2)
CAT 27607-77-8 Me3SiSO3CF3
PRO S 740801-32-5

RX(7) OF 82 ...C + T ===> U...

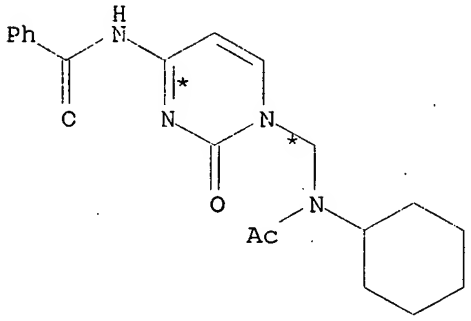



C




T

(7)



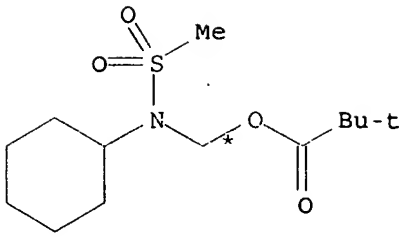

U
YIELD 72%

RX(7) RCT C 740801-28-9, T 26661-13-2

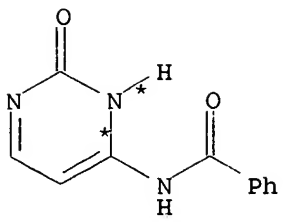
STAGE(1)
RGT K 10416-59-8 Me3SiN:CMeOSiMe3
SOL 75-05-8 MeCN

STAGE(2)
CAT 27607-77-8 Me3SiSO3CF3
PRO U 740801-33-6

RX(8) OF 82 ...G + T ===> V...

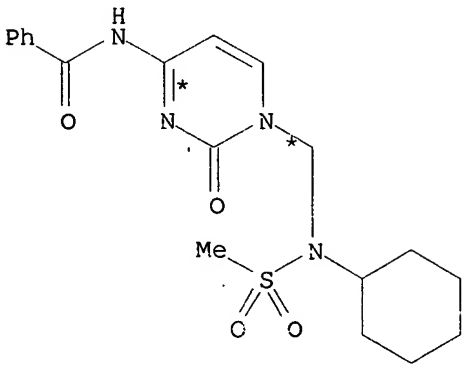


G



T

(8)



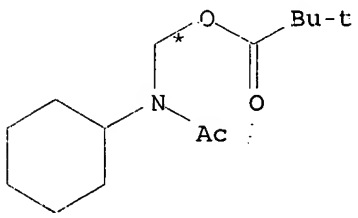
V
YIELD 56%

RX(8) RCT G 740801-29-0, T 26661-13-2

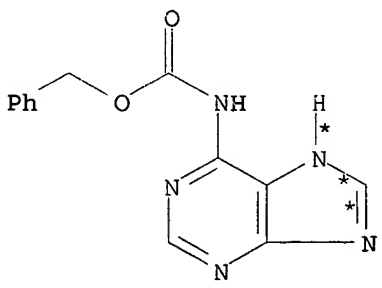
STAGE(1)
RGT K 10416-59-8 Me3SiN:CMeOSiMe3
SOL 75-05-8 MeCN

STAGE(2)
CAT 27607-77-8 Me3SiSO3CF3
PRO V 740801-34-7

RX(9) OF 82 ...C + H ===> W...

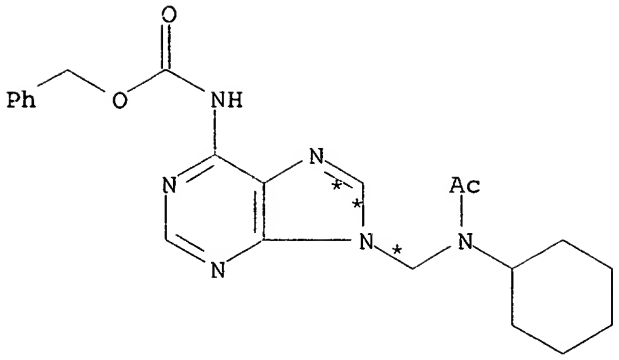


C



H

(9)



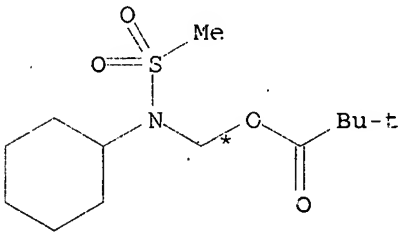
W
YIELD 58%

RX(9) RCT C 740801-28-9, H 82919-04-8

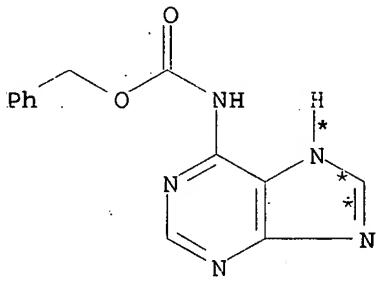
STAGE(1)
RGT K 10416-59-8 Me3SiN:CMeOSiMe3
SOL 75-05-8 MeCN

STAGE(2)
CAT 27607-77-8 Me3SiSO3CF3
PRO W 740801-35-8

RX(10) OF 82 ...G + H ===> X...

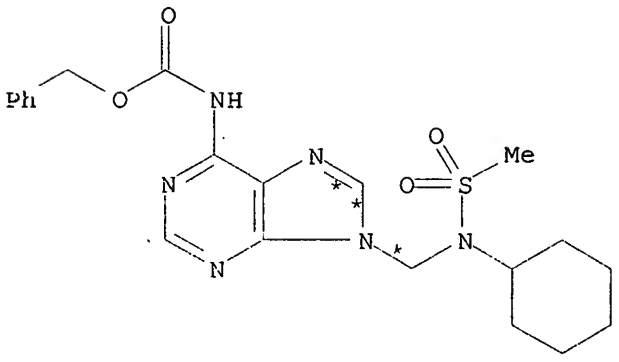


G



H

(10)



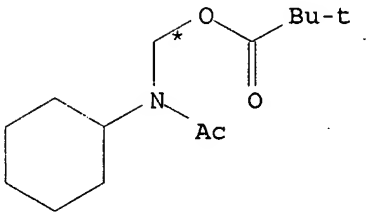
X
YIELD 22%

RX(10)  RCT  G 740801-29-0, H 82919-04-8

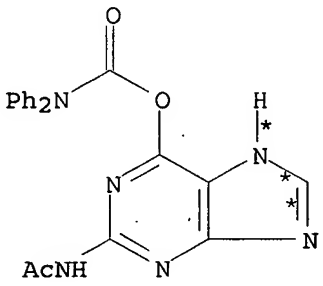
STAGE(1)
RGT  K 10416-59-8 Me3SiN:CMeOSiMe3
SOL  75-05-8 MeCN

STAGE(2)
CAT  27607-77-8 Me3SiSO3CF3
PRO  X 740801-36-9

RX(11) OF 82  ...C + Y ===> Z...

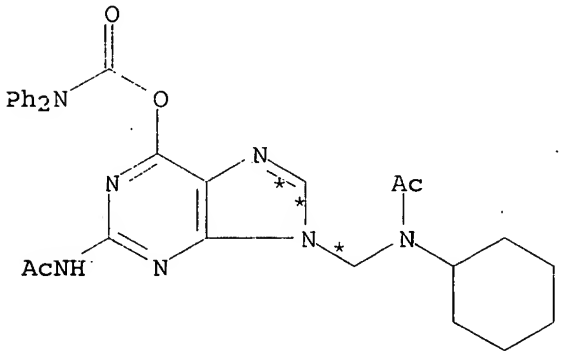


C



Y

(11)



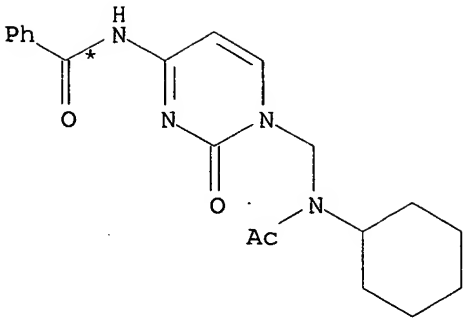
Z
YIELD 45%

RX(11)  RCT  C 740801-28-9, Y **112233-74-6**

STAGE(1)
RGT  K 10416-59-8 Me3SiN:CMeOSiMe3
SOL  75-05-8 MeCN

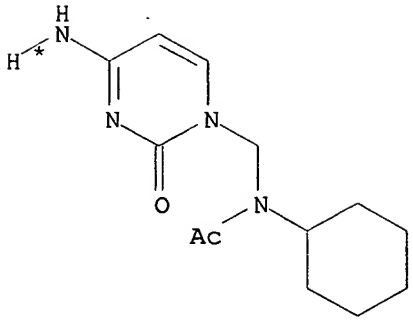
STAGE(2)
CAT  27607-77-8 Me3SiSO3CF3
PRO  Z **740801-37-0**

RX(12) OF 82  ...U ===> AA



U

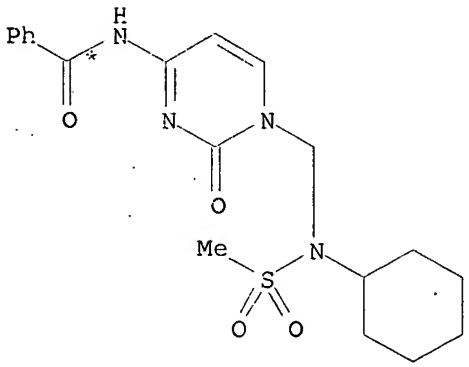
(12)



AA
YIELD 83%

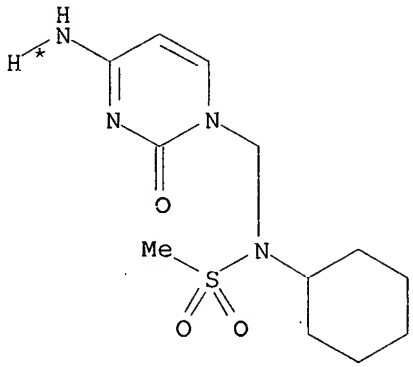
RX(12) RCT U 740801-33-6
RGT AB 7664-41-7 NH3
PRO AA 740801-38-1
SOL 7732-18-5 Water, 67-56-1 MeOH

RX(13) OF 82 ...V ===> AE



V

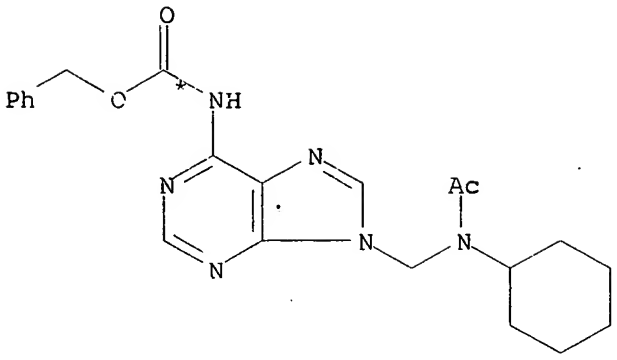
(13)



AE
YIELD 83%

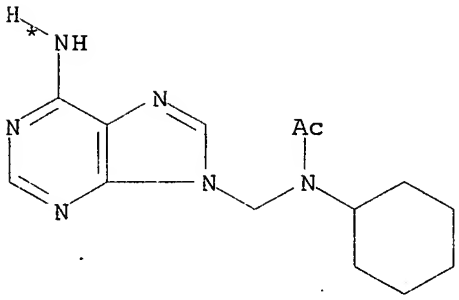
RX(13) RCT V 740801-34-7
RGT AB 7664-41-7 NH3
PRO AE 740801-39-2
SOL 7732-18-5 Water, 67-56-1 MeOH

RX(14) OF 82 ...W ===> AF



W

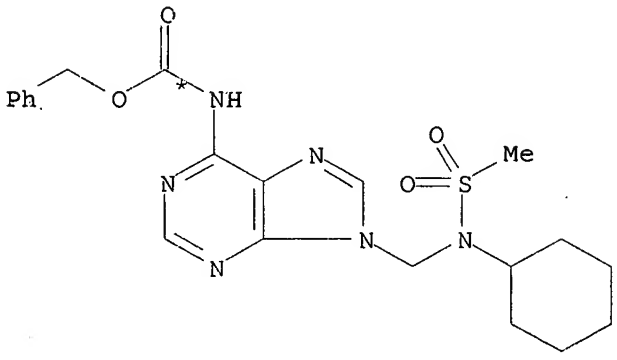
(14) ⟶



AF
YIELD 78%

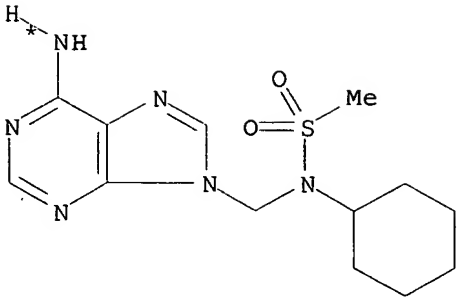
RX(14) RCT W 740801-35-8
RGT AG 1333-74-0 H2
PRO AF 740801-40-5
CAT 7440-05-3 Pd
SOL 67-56-1 MeOH

RX(15) OF 82 ...X ===> AI



X

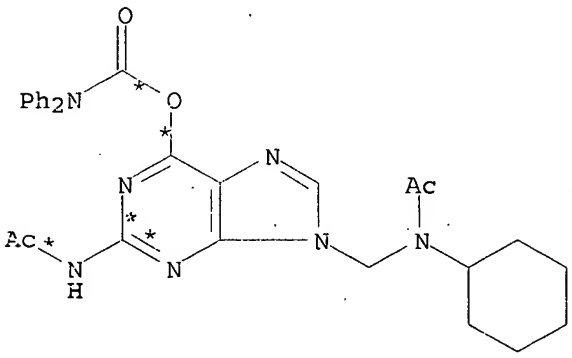
(15) ⟶



AI
YIELD 68%

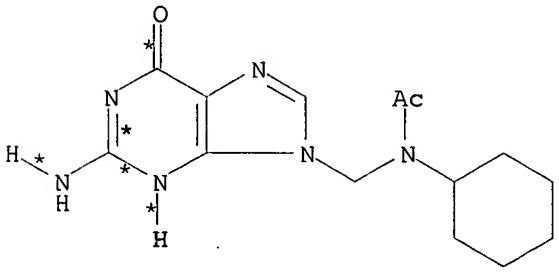
RX(15) RCT X 740801-36-9
RGT AG 1333-74-0 H2
PRO AI 740801-41-6
CAT 7440-05-3 Pd
SOL 67-56-1 MeOH

RX(16) OF 82 ...Z ===> AJ



Z

(16)



AJ
YIELD 81%

RX(16) RCT Z 740801-37-0

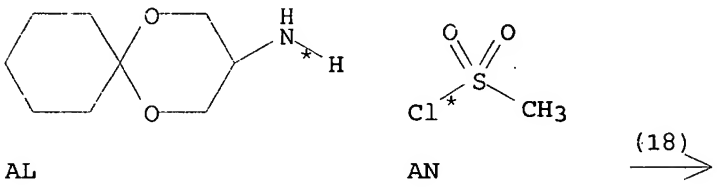
RGT AB 7664-41-7 NH3
PRO AJ 740801-42-7
SOL 7732-18-5 Water, 67-56-1 MeOH

RX(17) OF 82 AK ===> AL...

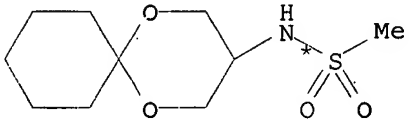
AK (17) AL
YIELD 100%

RX(17) RCT AK 125482-58-8
RGT AG 1333-74-0 H2
PRO AL 90950-23-5
CAT 7440-05-3 Pd
SOL 64-17-5 EtOH
NTE high pressure

RX(18) OF 82 ...AL + AN ===> AO...



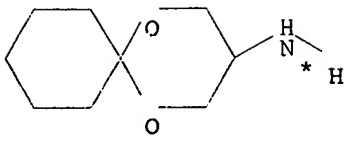
AL AN (18)



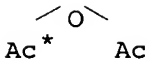
AO
YIELD 67%

RX(18) RCT AL 90950-23-5, AN 124-63-0
RGT AP 110-86-1 Pyridine
PRO AO 740801-44-9
SOL 75-09-2 CH2Cl2

RX(19) OF 82 ...AL + AR ===> AS...

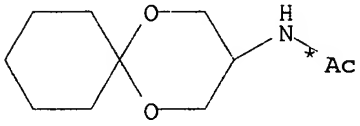


AL



AR

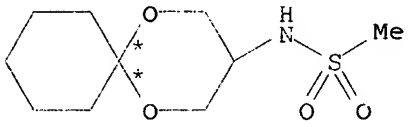
(19)



AS
YIELD 80%

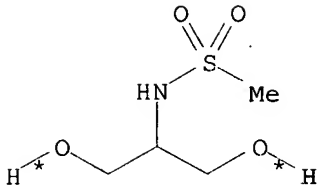
RX(19) RCT AL 90950-23-5, AR 108-24-7
PRO AS 740801-43-8

RX(20) OF 82 ...AO ===> AT...



AO

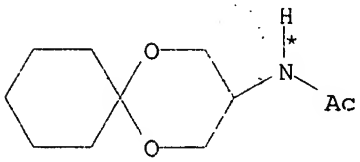
(20)



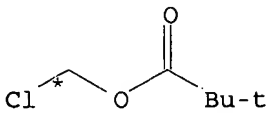
AT
YIELD 67%

RX(20) RCT AO 740801-44-9
RGT AU 11114-15-1 DOWEX 50W
PRO AT 740801-47-2
SOL 67-56-1 MeOH
NTE Dowex 50(H+) used

RX(21) OF 82 ...AS + B ===> AV



AS



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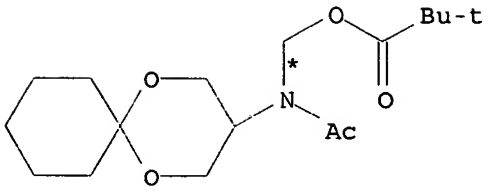
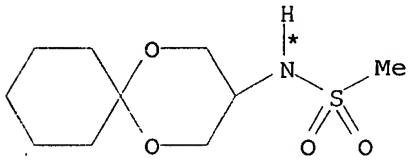


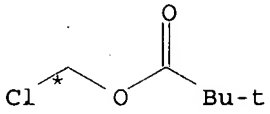
AV
YIELD 50%

RX(21) RCT AS 740801-43-8,. B 18997-19-8
RGT D 7646-69-7 NaH
PRO AV 740801-45-0
SOL 68-12-2 DMF

RX(22) OF 82 ...AO + B ===> AW



AO



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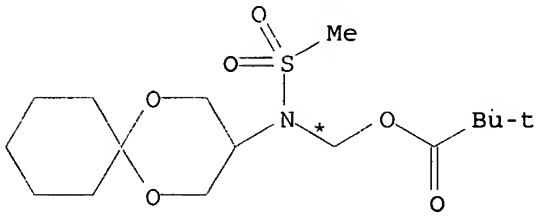
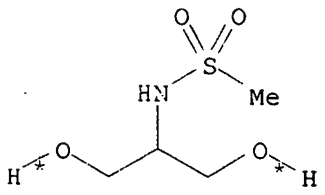


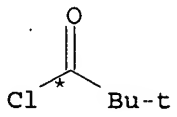
AW
YIELD 70%

RX(22) RCT AO 740801-44-9, B 18997-19-8
RGT D 7646-69-7 NaH
PRO AW 740801-46-1
SOL 68-12-2 DMF

RX(23) OF 82 ...AT + 2 AX ===> AY...

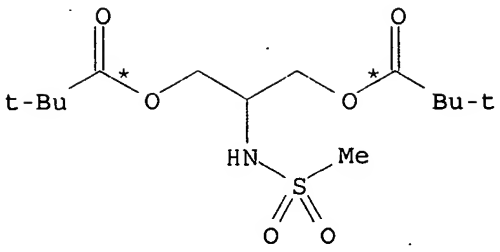


AT



2 AX

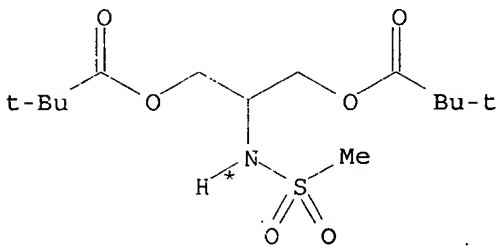
(23)



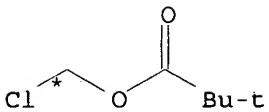
AY
YIELD 42%

RX(23) RCT AT 740801-47-2, AX 3282-30-2
PRO AY 740801-48-3
SOL 110-86-1 Pyridine

RX(24) OF 82 ...AY + B ===> I...



AY



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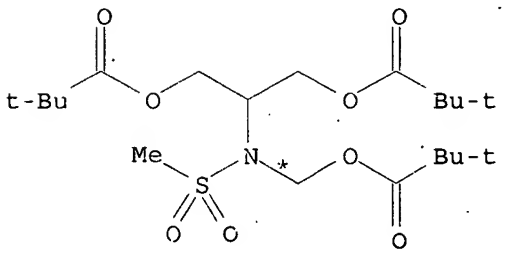
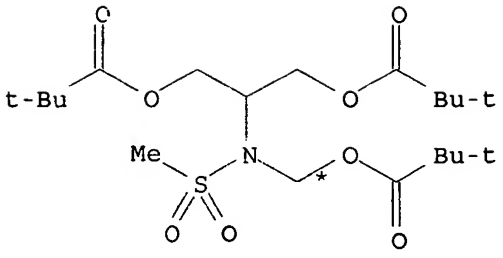


I
YIELD 88%

RX(24) RCT AY 740801-48-3, B 18997-19-8
RGT D 7646-69-7 NaH
PRO I 740801-49-4
SOL 68-12-2 DMF

RX(25) OF 82 ...I + T ===> AZ...



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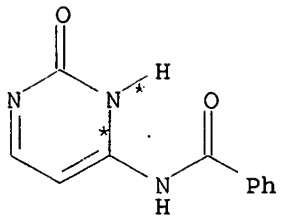

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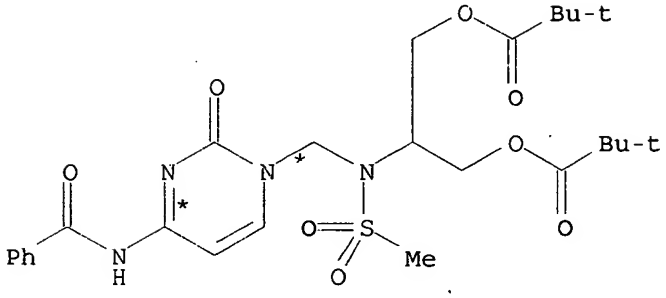
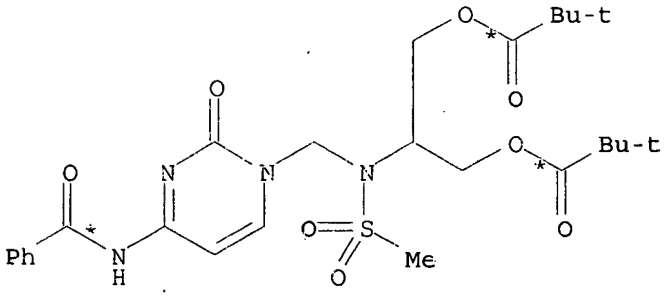


AZ
YIELD 71%

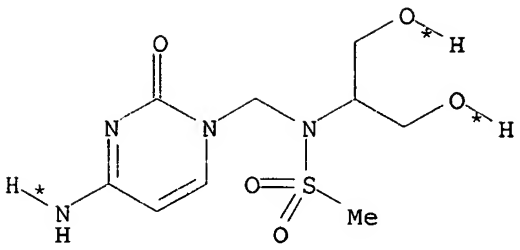
RX(25) RCT I 740801-49-4, T 26661-13-2
RGT K 10416-59-8 Me3SiN:CMeOSiMe3
PRO AZ 740801-50-7
CAT 27607-77-8 Me3SiSO3CF3
SOL 75-05-8 MeCN

RX(26) OF 82 ...AZ ===> BA



AZ

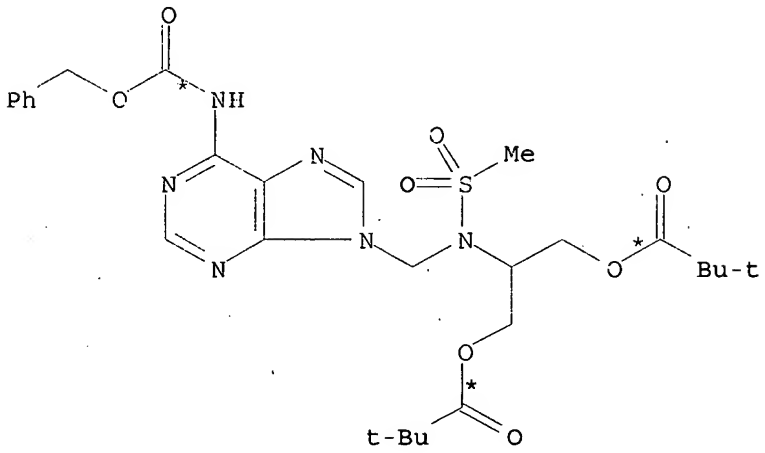
(26)



BA
YIELD 83%

RX(26) RCT AZ 740801-50-7
RGT AB 7664-41-7 NH3
PRO BA 740801-51-8
SOL 7732-18-5 Water, 67-56-1 MeOH

RX(27) OF 82 ...J ===> BB



J

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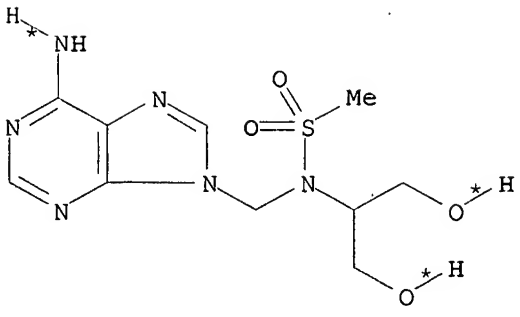

BB
YIELD 73%

RX(27) RCT J 740801-52-9

STAGE(1)
RGT AG 1333-74-0 H2
CAT 7440-05-3 Pd
SOL 67-56-1 MeOH

STAGE(2)
RGT AB 7664-41-7 NH3
SOL 7732-18-5 Water, 67-56-1 MeOH
PRO BB 740801-53-0

L2 ANSWER 11 OF 150 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 140:87057 CASREACT
TITLE: Benzyl vinylogous amide substituted aryldihydropyridazinones and aryldimethylpyrazolones as potent and selective PDE3B inhibitors
AUTHOR(S): Edmondson, Scott D.; Mastracchio, Anthony; He, Jiafang; Chung, Christine C.; Forrest, Michael J.; Hofsess, Scott; MacIntyre, Euan; Metzger, Joseph; O'Connor, Naphtali; Patel, Kajal; Tong, Xinchun; Tota, Michael R.; Van der Ploeg, Lex H. T.; Varnerin, Jeff P.; Fisher, Michael H.; Wyvratt, Matthew J.; Weber, Ann E.; Parmee, Emma R.
CORPORATE SOURCE: Department of Medicinal Chemistry, Merck & Co., Inc., Rahway, NJ, 07065, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(22), 3983-3987
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 1-3 (Pharmacology)
Section cross-reference(s): 28

ABSTRACT:
Aryldihydropyridazinones and aryldimethylpyrazolones with 2-benzyl vinylogous amide substituents have been identified as potent PDE3B subtype selective inhibitors. One dihydropyridazinone (PDE3B IC50=0.19 nM, 3A IC50=1.3 nM) was selected for in vivo evaluation of lipolysis induction, metabolic rate increase, and cardiovascular effects.

SUPPL. TERM: pyridazinone pyrazolone deriv prepn structure activity phosphodiesterase PDE3B
INDEX TERM: Structure-activity relationship
(enzyme-inhibiting; preparation and structure-activity relationship of benzyl vinylogous amide substituted aryldihydropyridazinones and aryldimethylpyrazolones as potent and selective PDE3B inhibitors)
INDEX TERM: Lipids, biological studies
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(lipolysis; preparation and structure-activity relationship of benzyl vinylogous amide substituted aryldihydropyridazinones and aryldimethylpyrazolones as potent and selective PDE3B inhibitors)
INDEX TERM: Antihypertensives
Vasodilators
(preparation and structure-activity relationship of benzyl vinylogous amide substituted aryldihydropyridazinones and aryldimethylpyrazolones as potent and selective PDE3B inhibitors)
INDEX TERM: 9036-21-9, Phosphodiesterase 3B
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)

(preparation and structure-activity relationship of benzyl vinylogous amide substituted aryldihydropyridazinones and aryldimethylpyrazolones as potent and selective PDE3B inhibitors)

INDEX TERM: 644984-68-9P
ROLE: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and structure-activity relationship of benzyl vinylogous amide substituted aryldihydropyridazinones and aryldimethylpyrazolones as potent and selective PDE3B inhibitors)

INDEX TERM: 81228-60-6P 220246-81-1P 644984-67-8P 644984-70-3P
644984-72-5P 644984-74-7P 644984-75-8P 644984-77-0P
644985-10-4P 644985-11-5P 644985-12-6P 644985-13-7P
644985-14-8P 644985-15-9P 644985-16-0P 644985-17-1P
644985-18-2P 644985-19-3P 644985-20-6P 644985-21-7P
644985-22-8P 644985-23-9P 644985-35-3P 644985-36-4P
644985-37-5P 644985-38-6P 644985-39-7P 644985-40-0P
644985-41-1P 644985-42-2P 644985-43-3P 644985-44-4P
644985-45-5P 644985-46-6P 644985-47-7P 644985-48-8P
ROLE: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and structure-activity relationship of benzyl vinylogous amide substituted aryldihydropyridazinones and aryldimethylpyrazolones as potent and selective PDE3B inhibitors)

INDEX TERM: 68550-75-4, Cilostamide 78415-72-2, Milrinone
ROLE: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation and structure-activity relationship of benzyl vinylogous amide substituted aryldihydropyridazinones and aryldimethylpyrazolones as potent and selective PDE3B inhibitors)

INDEX TERM: 75-36-5, Acetyl chloride 100-39-0, Benzyl bromide
312-94-7, Benzoyl chloride, 2-(trifluoromethyl)- 501-53-1, Carbonochloridic acid, phenylmethyl ester 541-41-3, Carbonochloridic acid, ethyl ester 547-63-7, Propanoic acid, 2-methyl-, methyl ester 586-76-5 600-00-0, Propanoic acid, 2-bromo-2-methyl-, ethyl ester 767-00-0
1122-91-4 1193-55-1, 1,3-Cyclohexanedione 3336-16-1
6165-69-1, Boronic acid, 3-thienyl- 7697-28-1
13331-27-6, Boronic acid, (3-nitrophenyl)- 14143-26-1
22381-56-2, 1,3-Cyclohexanedione, 2-(phenylmethyl)-
24078-12-4 28314-82-1 57848-46-1 59748-90-2
68837-59-2 82380-18-5 101328-85-2 112704-79-7
126162-38-7 153556-42-4 158435-41-7 266306-27-8
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644984-88-3 644984-89-4 644984-90-7 644984-91-8
644984-92-9 644984-93-0 644984-94-1 644985-24-0
724453-04-7 724453-07-0 724453-16-1 724453-25-2
724454-33-5 724455-21-4 724456-36-4
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(preparation and structure-activity relationship of benzyl vinylogous amide substituted aryldihydropyridazinones and aryldimethylpyrazolones as potent and selective PDE3B inhibitors)

INDEX TERM: 621-84-1, Carbamic acid, phenylmethyl ester
ROLE: RCT (Reactant); RGT (Reagent); RACT (Reactant or reagent)
(preparation and structure-activity relationship of benzyl vinylogous amide substituted aryldihydropyridazinones and

aryldimethylpyrazolones as potent and selective PDE3B inhibitors)

INDEX TERM: 150424-74-1P 644984-79-2P 644984-80-5P 644984-81-6P
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644985-52-4P 644985-53-5P 644985-54-6P 644985-55-7P
644985-56-8P 644985-57-9P 644985-58-0P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and structure-activity relationship of benzyl vinylogous amide substituted aryldihydropyridazinones and aryldimethylpyrazolones as potent and selective PDE3B inhibitors)

INDEX TERM: 644984-68-9DP, derivs.
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(preparation and structure-activity relationship of benzyl vinylogous amide substituted aryldihydropyridazinones and aryldimethylpyrazolones as potent and selective PDE3B inhibitors)

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD.

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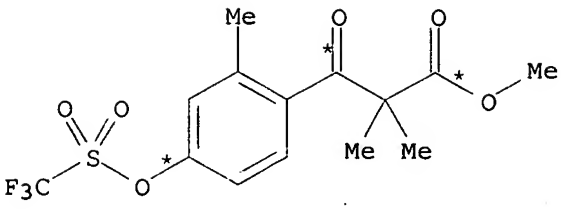
RX(1) OF 205 ...A + B ===> C



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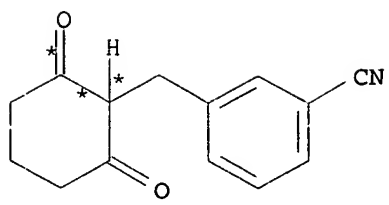
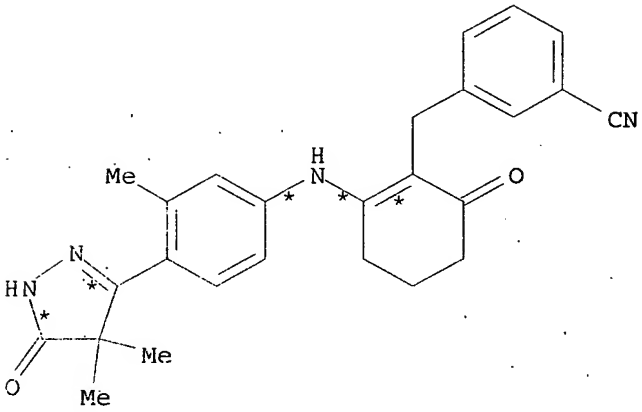


B

(1)



C

RX(1) RCT A 644985-55-7

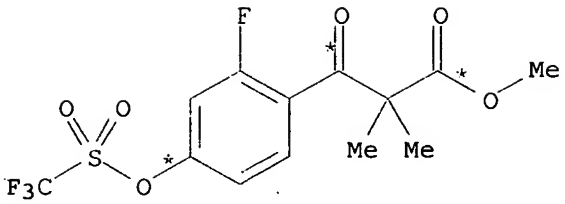
STAGE(1)
RGT D 621-84-1 Carbamic acid, phenylmethyl ester, E 534-17-8 Cs2CO3
CAT 51364-51-3 Ph2-pentadienone Pd, 161265-03-8 Phosphine, (9,9-dimethyl-9H-xanthene-4,5-diyl)bis[diphenyl-
SOL 109-99-9 THF

STAGE(2)
RGT F 302-01-2 N2H4
SOL 64-17-5 EtOH

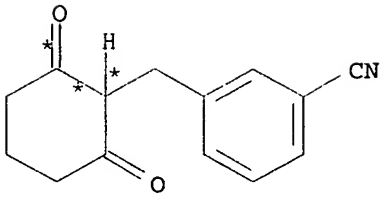
STAGE(3)
RGT G 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(4)
RCT B 724453-04-7
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe, 67-68-5 DMSO
PRO C 644985-37-5
NTE Buchwald reaction first stage, alternate prepn. also described

RX(2) OF 205 ...P + B ===> Q



P



B

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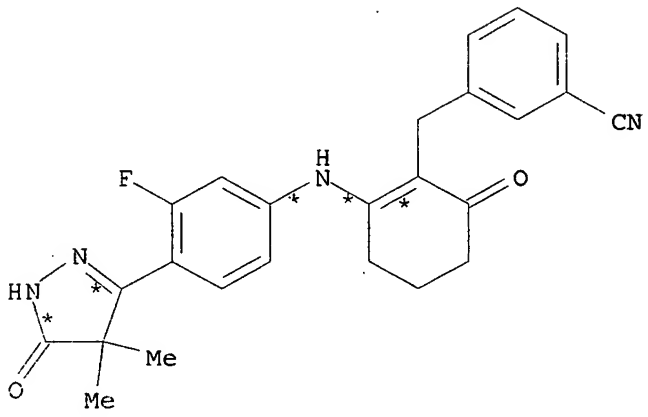


Q

RX(2) RCT P 644985-56-8

STAGE(1)
RGT D 621-84-1 Carbamic acid, phenylmethyl ester, E 534-17-8 Cs2CO3
CAT 51364-51-3 Ph2-pentadienone Pd, 161265-03-8 Phosphine, (9,9-dimethyl-9H-xanthene-4,5-diyl)bis[diphenyl-
SOL 109-99-9 THF

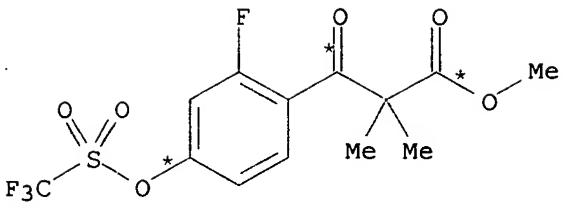
STAGE(2)
RGT F 302-01-2 N2H4
SOL 64-17-5 EtOH

STAGE(3)
RGT G 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

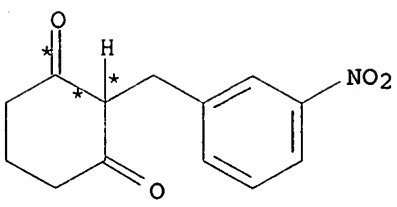
STAGE(4)
RCT B 724453-04-7
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe, 67-68-5 DMSO

PRO Q 644985-39-7
NTE Buchwald reaction first stage, alternate prepn. also described

RX(3) OF 205 ...P + R ===> S

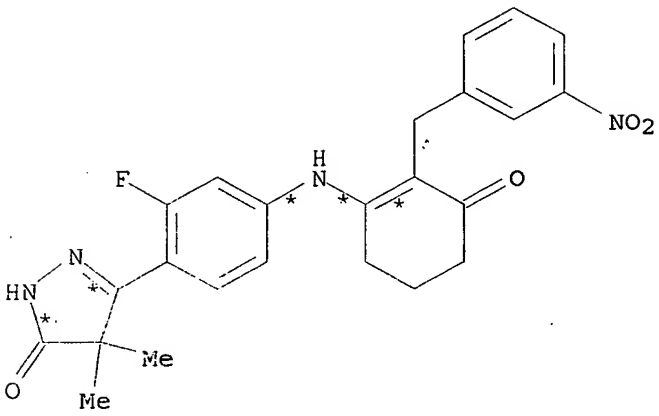


P



R

(3)



S

RX(3) RCT P 644985-56-8

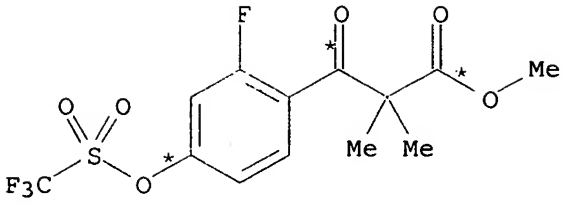
STAGE(1)
RGT D 621-84-1 Carbamic acid, phenylmethyl ester, E 534-17-8
Cs2CO3
CAT 51364-51-3 Ph2-pentadienone Pd, 161265-03-8 Phosphine,
(9,9-dimethyl-9H-xanthene-4,5-diyl)bis[diphenyl-
SOL 109-99-9 THF

STAGE(2)
RGT F 302-01-2 N2H4
SOL 64-17-5 EtOH

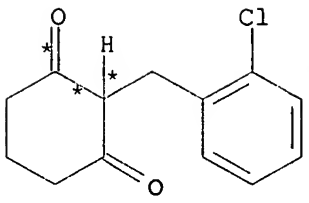
STAGE(3)
RGT G 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(4)
RCT R 724453-07-0
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe, 67-68-5 DMSO
PRO S 644985-40-0
NTE Buchwald reaction first stage, alternate prepn. also described

RX(4) OF 205 ...P + T ===> U

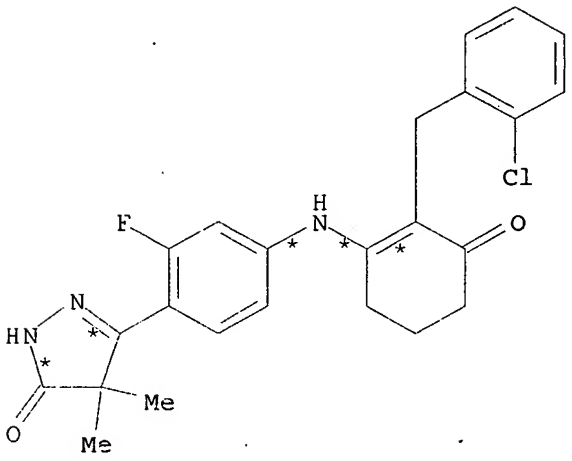


P



T

(4) →



U

RX(4) RCT P 644985-56-8

STAGE(1)
RGT D 621-84-1 Carbamic acid, phenylmethyl ester, E 534-17-8 Cs2CO3
CAT 51364-51-3 Ph2-pentadienone Pd, 161265-03-8 Phosphine, (9,9-dimethyl-9H-xanthene-4,5-diyl)bis[diphenyl-
SOL 109-99-9 THF

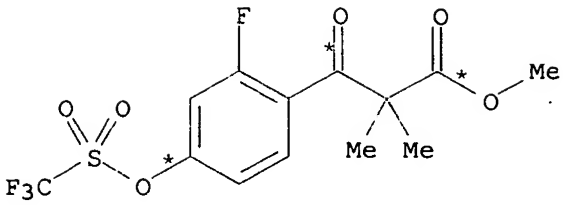
STAGE(2)
RGT F 302-01-2 N2H4
SOL 64-17-5 EtOH

STAGE(3)
RGT G 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

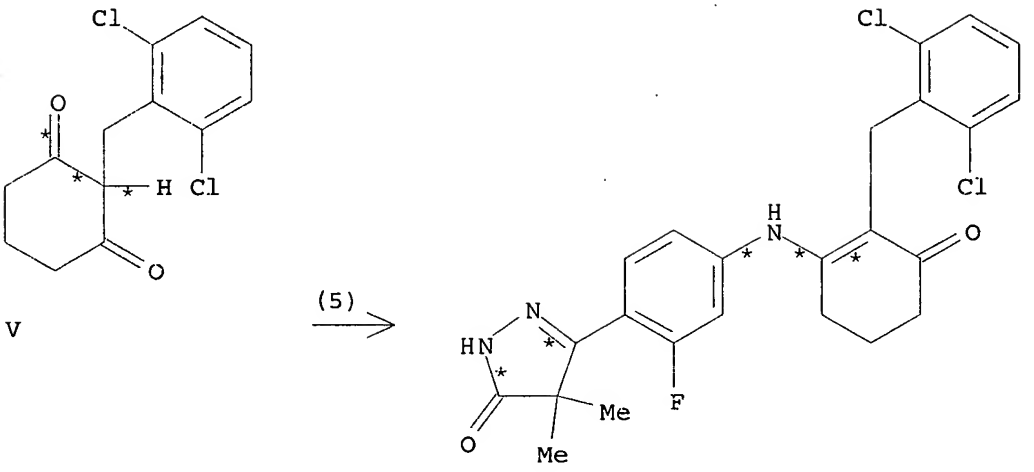
STAGE(4)
RCT T 724453-16-1
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe, 67-68-5 DMSO

PRO U 644985-41-1
NTE Buchwald reaction first stage, alternate prepn. also described

RX(5) OF 205 ...P + V ===> W



P



V

W

RX(5) RCT P 644985-56-8

STAGE(1)
RGT D 621-34-1 Carbamic acid, phenylmethyl ester, E 534-17-8 Cs2CO3
CAT 51364-51-3 Ph2-pentadienone Pd, 161265-03-8 Phosphine, (9,9-dimethyl-9H-xanthene-4,5-diyl)bis[diphenyl-
SOL 109-99-9 THF

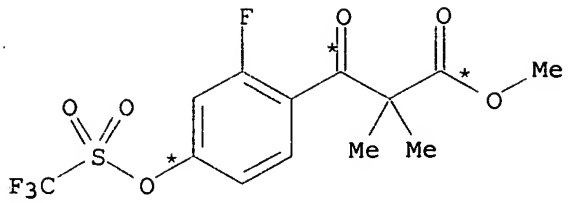
STAGE(2)
RGT F 302-01-2 N2H4
SOL 64-17-5 EtOH

STAGE(3)
RGT G 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

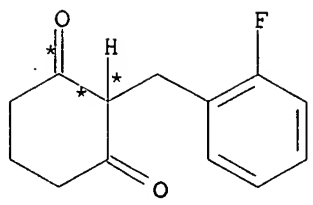
STAGE(4)
RCT V 724453-25-2
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe, 67-68-5 DMSO

PRO W 644985-42-2
NTE Buchwald reaction first stage, alternate prepn. also described

RX(6) OF 205 ...P + X ===> Y

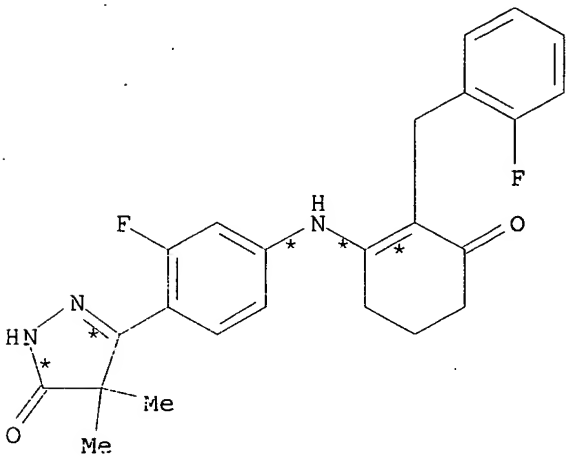


P



X

(6) ⟶



Y

RX(6) RCT P 644985-56-8

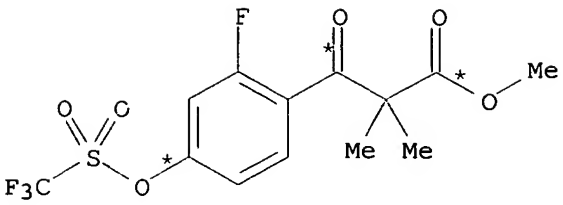
STAGE(1)
RGT D 621-84-1 Carbamic acid, phenylmethyl ester, E 534-17-8 Cs2CO3
CAT 51364-51-3 Ph2-pentadienone Pd, 161265-03-8 Phosphine, (9,9-dimethyl-9H-xanthene-4,5-diyl)bis[diphenyl-
SOL 109-99-9 THF

STAGE(2)
RGT F 302-01-2 N2H4
SOL 64-17-5 EtOH

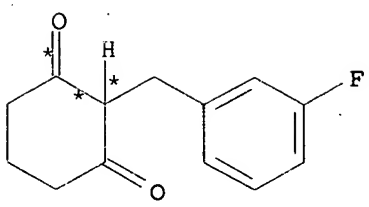
STAGE(3)
RGT G 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(4)
RCT X 724454-33-5
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe, 67-68-5 DMSO
PRO Y 644985-43-3
NTE Buchwald reaction first stage, alternate prepn. also described

RX(7) OF 205 ...P + Z ===> AA

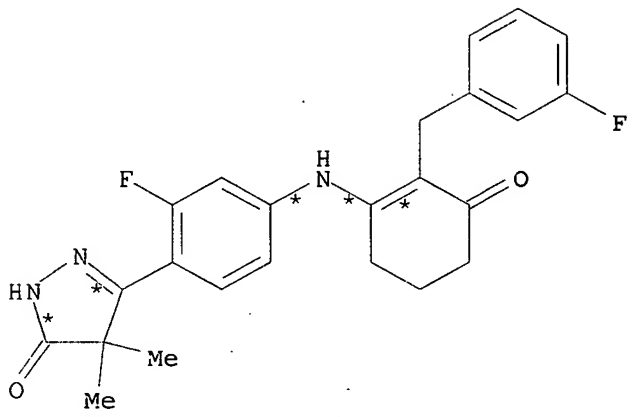


P



Z

(7) →



AA

RX(7) RCT P 644985-56-8

STAGE(1)
RGT D 621-84-1 Carbamic acid, phenylmethyl ester, E 534-17-8 Cs2CO3
CAT 51364-51-3 Ph2-pentadienone Pd, 161265-03-8 Phosphine, (9,9-dimethyl-9H-xanthene-4,5-diyl)bis[diphenyl-
SOL 109-99-9 THF

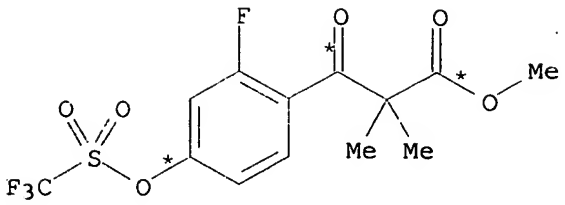
STAGE(2)
RGT F 302-01-2 N2H4
SOL 64-17-5 EtOH

STAGE(3)
RGT G 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

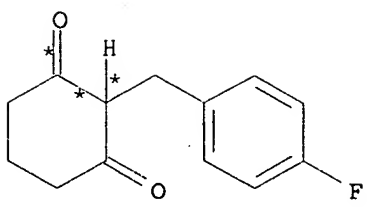
STAGE(4)
RCT Z 724455-21-4
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe, 67-68-5 DMSO

PRO AA 644985-44-4
NTE Buchwald reaction first stage, alternate prepn. also described

RX(8) OF 205 ...P + AB ===> AC

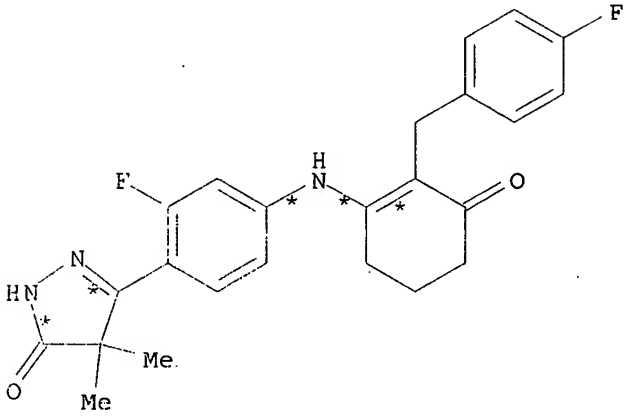


P



AB

(8)



AC

RX(8) RCT P 644985-56-8

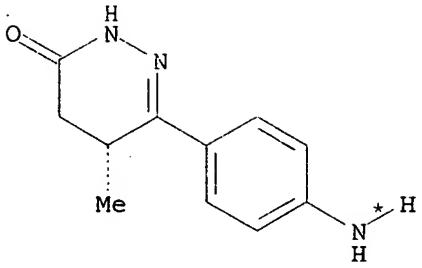
STAGE(1)
RGT D 621-84-1 Carbamic acid, phenylmethyl ester, E 534-17-8 Cs2CO3
CAT 51364-51-3 Ph2-pentadienone Pd, 161265-03-8 Phosphine, (9,9-dimethyl-9H-xanthene-4,5-diyl)bis[diphenyl-
SOL 109-99-9 THF

STAGE(2)
RGT F 302-01-2 N2H4
SOL 64-17-5 EtOH

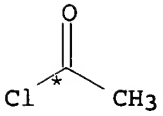
STAGE(3)
RGT G 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(4)
RCT AB 724456-36-4
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe, 67-68-5 DMSO
PRO AC 644985-45-5
NTE Buchwald reaction first stage, alternate prepn. also described

RX(9) OF 205 AD + AE ===> AF

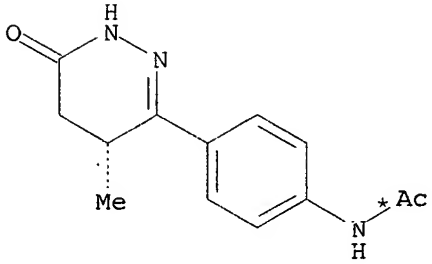


AD



AE

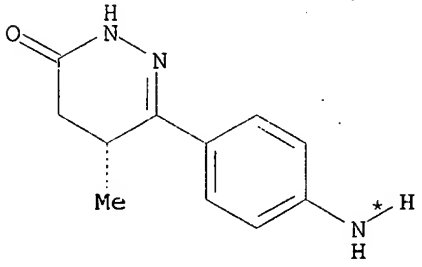
(9)



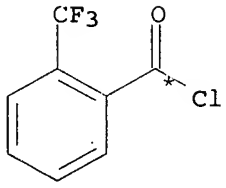
AF

RX(9) RCT AD 101328-85-2, AE 75-36-5
RGT AG 121-44-8 Et3N
PRO AF 220246-81-1
SOL 75-09-2 CH2Cl2

RX(10) OF 205 AD + AI ===> AJ

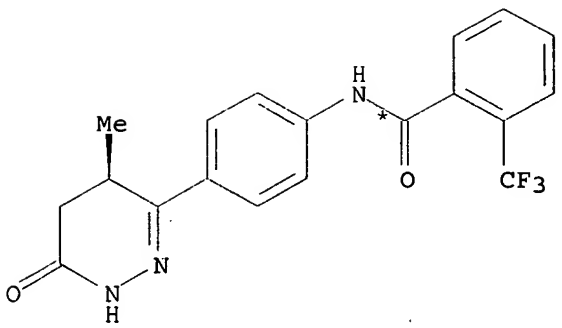


AD



AI

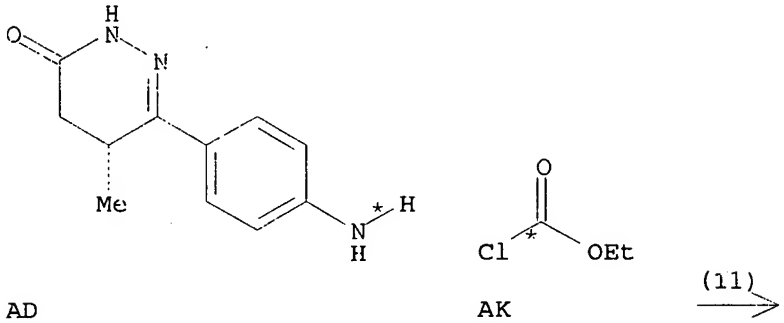
(10)



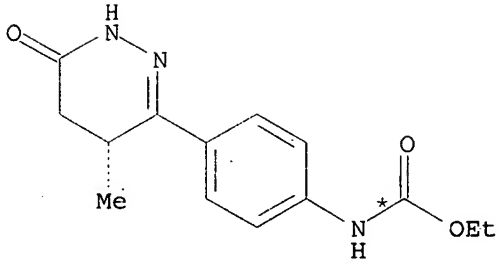
AJ

RX(10) RCT AD 101328-85-2, AI 312-94-7
RGT AG 121-44-8 Et3N
PRO AJ 644984-70-3
SOL 75-09-2 CH2Cl2

RX(11) OF 205 AD + AK ===> AL



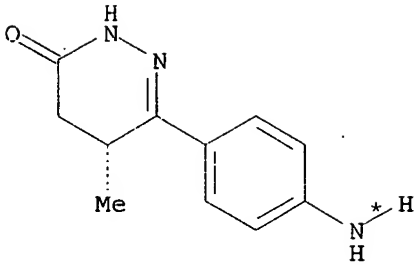
AD AK (11)



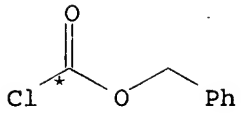
AL

RX(11) RCT AD 101328-85-2, AK 541-41-3
RGT AG 121-44-8 Et3N
PRO AL 644984-72-5
SOL 75-09-2 CH2Cl2

RX(12) OF 205 AD + AM ===> AN

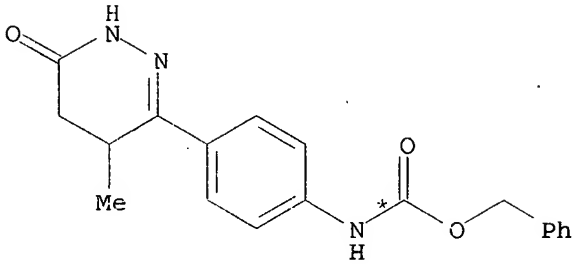


AD



AM

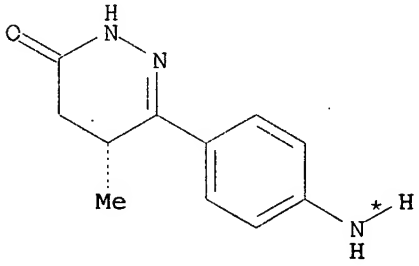
(12)



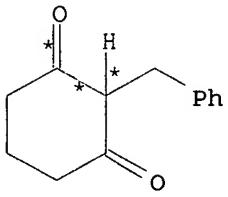
AN

RX(12) RCT AD 101328-85-2, AM 501-53-1
RGT AG 121-44-8 Et3N
PRO AN 81228-60-6
SOL 75-09-2 CH2Cl2

RX(13) OF 205 AD + AO ===> AP

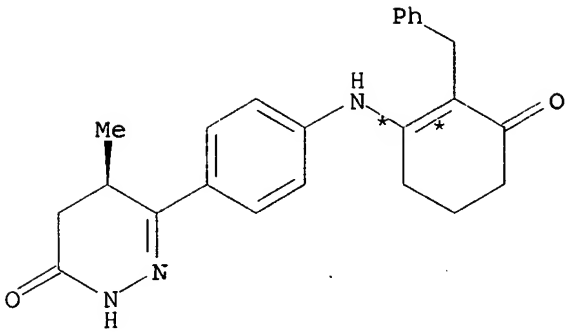


AD



AO

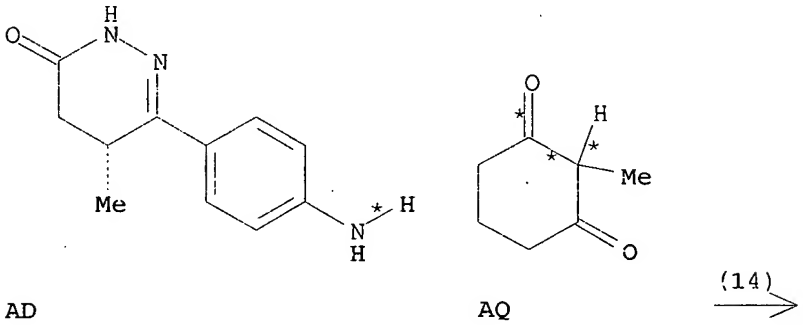
(13)



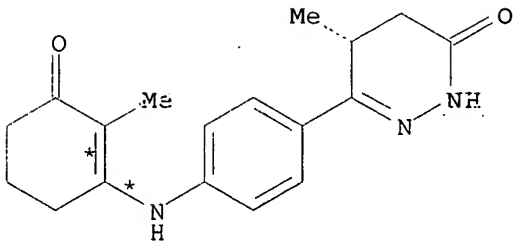
AP

RX(13) RCT AD 101328-85-2, AO 22381-56-2
PRO AP 644984-68-9
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe, 67-68-5 DMSO

RX(14) OF 205 AD + AQ ===> AR



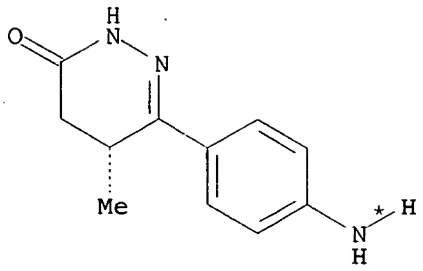
AD AQ (14)



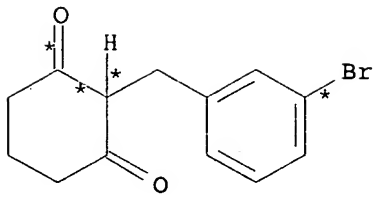
AR

RX(14) RCT AD 101328-85-2, AQ 1193-55-1
PRO AR 644984-74-7
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe, 67-68-5 DMSO

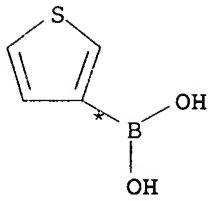
RX(15) OF 205 AD + AS + AT ===> AU



AD

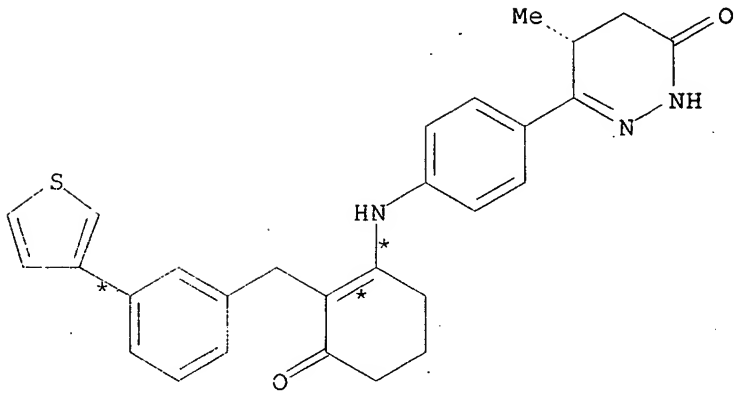


AS



AT

(15)



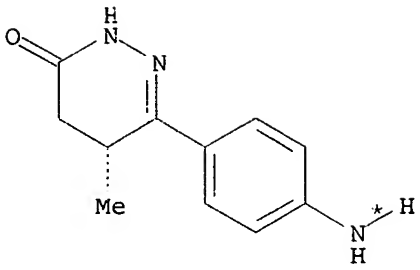
AU

RX(15) RCT AD 101328-85-2, AS 644984-66-7

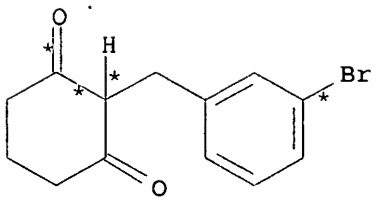
STAGE(1)
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe, 67-68-5 DMSO

STAGE(2)
RCT AT 6165-69-1
RGT AV 497-19-8 Na2CO3
CAT 14221-01-3 Pd(PPh3)4
SOL 7732-18-5 Water, 64-17-5 EtOH, 123-91-1 Dioxane
PRO AU 644984-75-8
NTE Suzuki reaction second stage

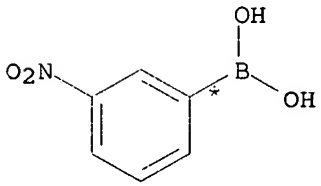
RX(16) OF 205 AD + AS + AZ ===> BA



AD

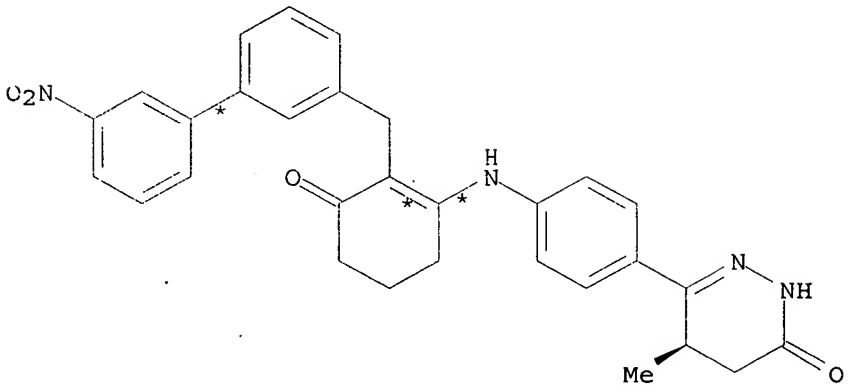


AS



AZ

(16)



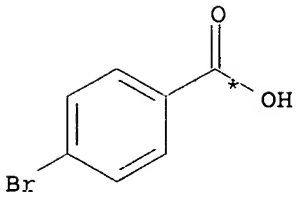
BA

RX(16) RCT AD 101328-85-2, AS 644984-66-7

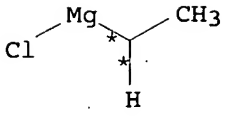
STAGE(1)
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe, 67-68-5 DMSO

STAGE(2)
RCT AZ 13331-27-6
RGT AV 497-19-8 Na2CO3
CAT 14221-01-3 Pd(PPh3)4
SOL 7732-18-5 Water, 64-17-5 EtOH, 123-91-1 Dioxane
PRO BA 644984-77-0
NTE Suzuki reaction second stage

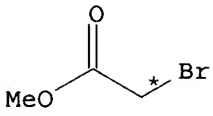
RX(17) OF 205 BB + BC + BD ===> BE...



BB

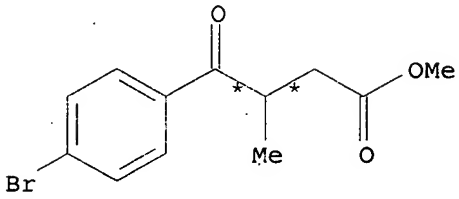


BC



BD

(17)



BE

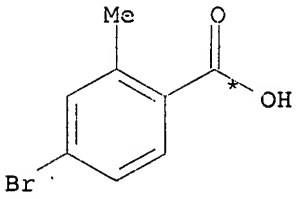
RX(17) RCT BB 586-76-5

STAGE(1)
RGT BF 6638-79-5 MeNHOMe-HCl, BG 2592-95-2 1-Benzotriazolol, BH 25952-53-8 EDAP, BI 7087-68-5 EtN(Pr-i)2
SOL 75-09-2 CH2Cl2

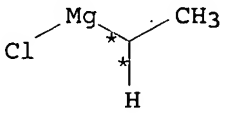
STAGE(2)
RCT BC 2386-64-3
SOL 109-99-9 THF

STAGE(3)
RCT BD 96-32-2
RGT BJ 4039-32-1 (Me3Si)2N.Li
SOL 109-99-9 THF
PRO BE 150424-74-1
NTE Grignard reaction second stage

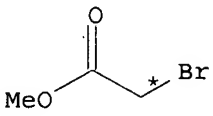
RX(18) OF 205 BK + BC + BD ===> BL...



BK

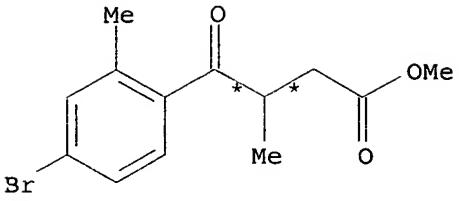


BC



BD

(18)



BL

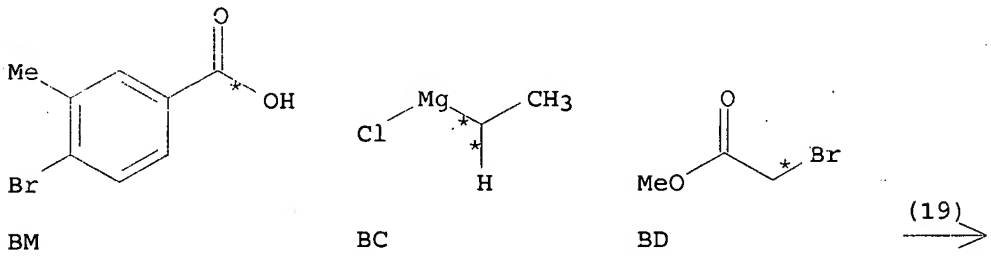
RX(18) RCT BK 68837-59-2

STAGE(1)
RGT BF 6638-79-5 MeNHOMe-HCl, BG 2592-95-2 1-Benzotriazolol, BH 25952-53-8 EDAP, BI 7087-68-5 EtN(Pr-i)2
SOL 75-09-2 CH2Cl2

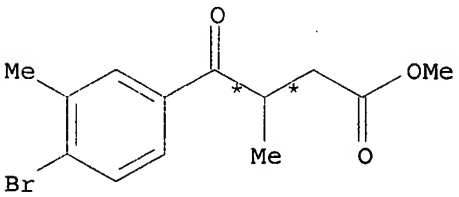
STAGE(2)
RCT BC 2386-64-3
SOL 109-99-9 THF

STAGE(3)
RCT BD 96-32-2
RGT BJ 4039-32-1 (Me3Si)2N.Li
SOL 109-99-9 THF
PRO BL 644984-79-2
NTE Grignard reaction second stage

RX(19) OF 205 BM + BC + BD ===> BN...



BM BC BD



BN

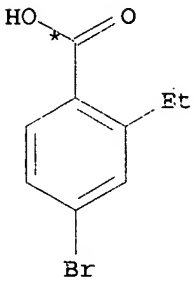
RX(19) RCT BM 7697-28-1

STAGE(1)
RGT BF 6638-79-5 MeNHOMe-HCl, BG 2592-95-2 1-Benzotriazolol, BH 25952-53-8 EDAP, BI 7087-68-5 EtN(Pr-i)2
SOL 75-09-2 CH2Cl2

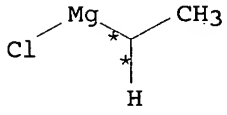
STAGE(2)
RCT BC 2386-64-3
SOL 109-99-9 THF

STAGE(3)
RCT BD 96-32-2
RGT BJ 4039-32-1 (Me3Si)2N.Li
SOL 109-99-9 THF
PRO BN 644984-80-5
NTE Grignard reaction second stage

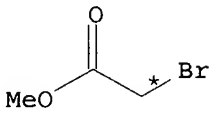
RX(20) OF 205 BO + BC + BD ===> BP...



BO

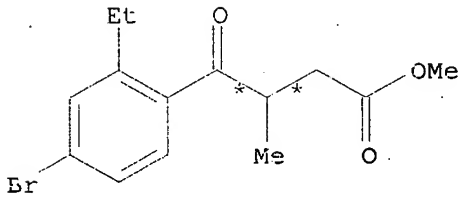


BC



BD

(20)



BP

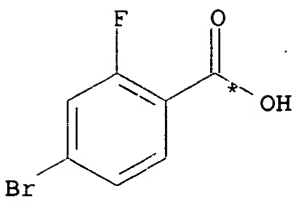
RX(20) RCT BO 644984-78-1

STAGE(1)
RGT BF 6638-79-5 MeNHOMe-HCl, BG 2592-95-2 1-Benzotriazolol, BH 25952-53-8 EDAP, BI 7087-68-5 EtN(Pr-i)2
SOL 75-09-2 CH2Cl2

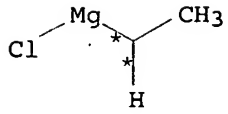
STAGE(2)
RCT BC 2386-64-3
SOL 109-99-9 THF

STAGE(3)
RCT BD 96-32-2
RGT BJ 4039-32-1 (Me3Si)2N.Li
SOL 109-99-9 THF
PRO BP 644984-81-6
NTE Grignard reaction second stage

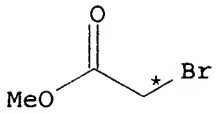
RX(21) OF 205 BQ + BC + BD ===> BR...



BQ

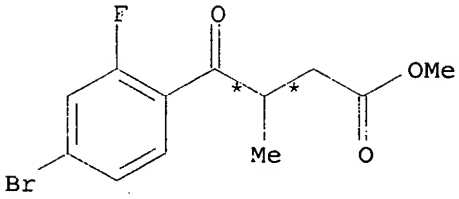


BC



BD

(21)



BR

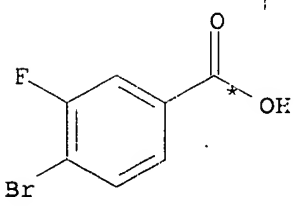
RX(21) RCT BQ 112704-79-7

STAGE(1)
RGT BF 6638-79-5 MeNHOMe-HCl, BG 2592-95-2 1-Benzotriazolol, BH 25952-53-8 EDAP, BI 7087-68-5 EtN(Pr-i)2
SOL 75-09-2 CH2Cl2

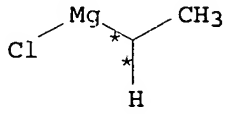
STAGE(2)
RCT BC 2386-64-3
SOL 109-99-9 THF

STAGE(3)
RCT BD 96-32-2
RGT BJ 4039-32-1 (Me3Si)2N.Li
SOL 109-99-9 THF
PRO BR 644984-82-7
NTE Grignard reaction second stage

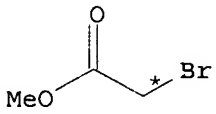
RX(22) OF 205 BS + BC + BD ===> BT...



BS

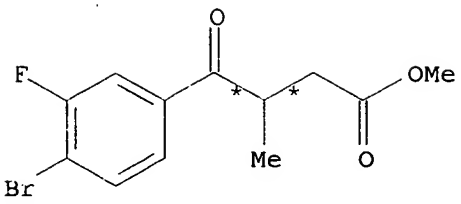


BC



BD

(22)



BT

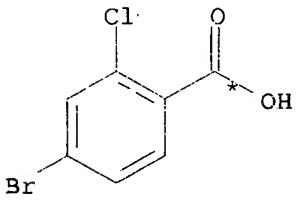
RX(22)  RCT  BS 153556-42-4

STAGE(1)
RGT  BF 6638-79-5 MeNHOMe-HCl, BG 2592-95-2 1-Benzotriazolol, BH 25952-53-8 EDAP, BI 7087-68-5 EtN(Pr-i)2
SOL  75-09-2 CH2Cl2

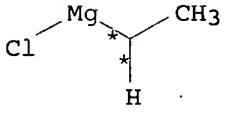
STAGE(2)
RCT  BC 2386-64-3
SOL  109-99-9 THF

STAGE(3)
RCT  BD 96-32-2
RGT  BJ 4039-32-1 (Me3Si)2N.Li
SOL  109-99-9 THF
PRO  BT 644984-83-8
NTE  Grignard reaction second stage

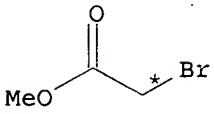
RX(23) OF 205  BU + BC + BD ===> BV...



BU

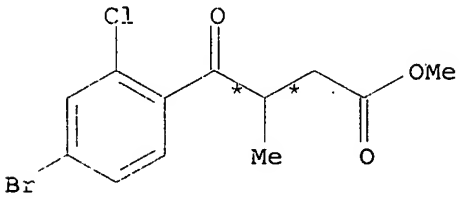


BC



BD

(23)



BV

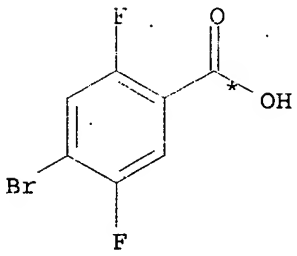
RX(23)  RCT  BU 59748-90-2

STAGE(1)
RGT  BF 6638-79-5 MeNHOMe-HCl, BG 2592-95-2 1-Benzotriazolol, BH 25952-53-8 EDAP, BI 7087-68-5 EtN(Pr-i)2
SOL  75-09-2 CH2Cl2

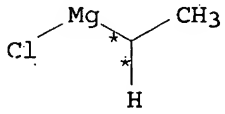
STAGE(2)
RCT BC 2386-64-3
SOL 109-99-9 THF

STAGE(3)
RCT BD 96-32-2
RGT BJ 4039-32-1 (Me3Si)2N.Li
SOL 109-99-9 THF
PRO BV 644984-84-9
NTE Grignard reaction second stage

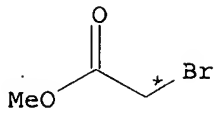
RX(24) OF 205 BW + BC + BD ===> BX...



BW

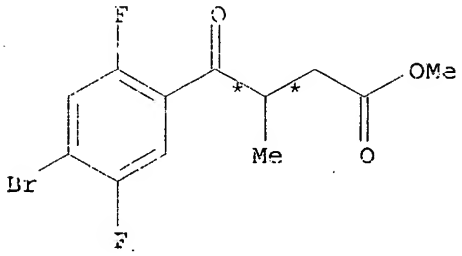


BC



BD

(24)



BX

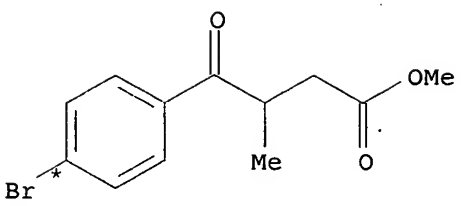
RX(24) RCT BW 28314-82-1

STAGE(1)
RGT BF 6638-79-5 MeNHOMe-HCl, BG 2592-95-2 1-Benzotriazolol, BH 25952-53-8 EDAP, BI 7087-68-5 EtN(Pr-i)2
SOL 75-09-2 CH2Cl2

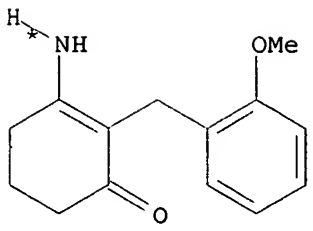
STAGE(2)
RCT BC 2386-64-3
SOL 109-99-9 THF

STAGE(3)
RCT BD 96-32-2
RGT BJ 4039-32-1 (Me3Si)2N.Li
SOL 109-99-9 THF
PRO BX 644984-85-0
NTE Grignard reaction second stage

RX(25) OF 205 ...BE + BY ===> BZ...

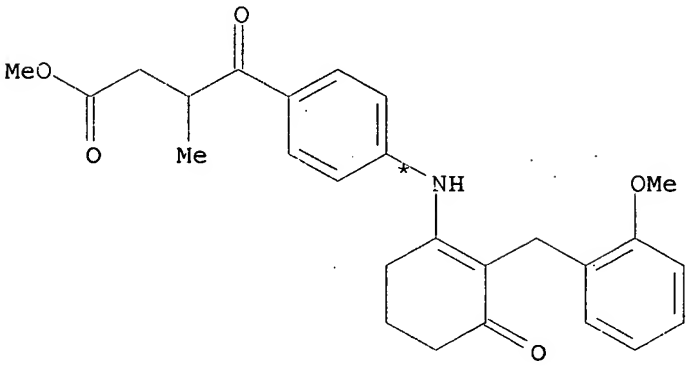


BE



BY

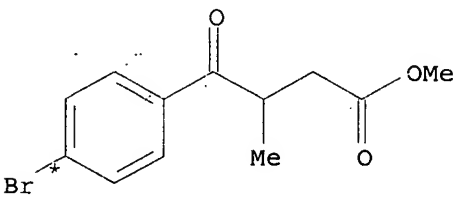
(25)



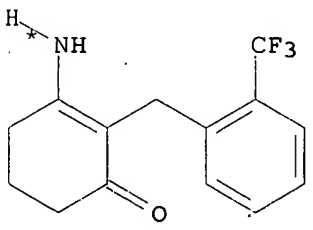
BZ

RX(25) RCT BE 150424-74-1, BY 644984-86-1
RGT E 534-17-8 Cs2CO3
PRO BZ 644984-95-2
CAT 51364-51-3 Ph2-pentadienone Pd, 213697-53-1 [1,1'-Biphenyl]-2-amine, 2'-(dicyclohexylphosphino)-N,N-dimethyl-
SOL 109-99-9 THF
NTE Buchwald reaction

RX(26) OF 205 ...BE + CB ===> CC...

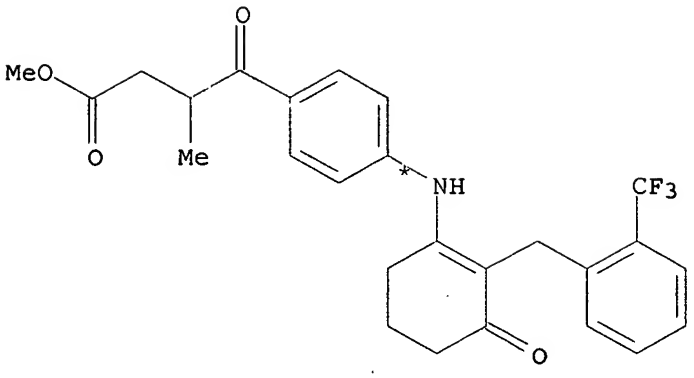


BE



CB

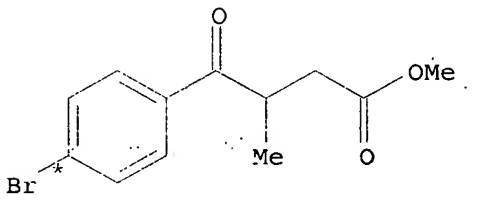
(26)



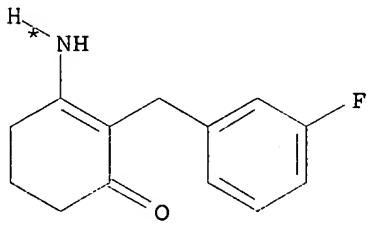
CC

RX(26) RCT BE 150424-74-1, CB 644984-87-2
RGT E 534-17-8 Cs2CO3
PRO CC 644984-96-3
CAT 51364-51-3 Ph2-pentadienone Pd, 213697-53-1 [1,1'-Biphenyl]-2-amine, 2'-(dicyclohexylphosphino)-N,N-dimethyl-
SOL 109-99-9 THF
NTE Buchwald reaction

RX(27) OF 205 ...BE + CD ===> CE...

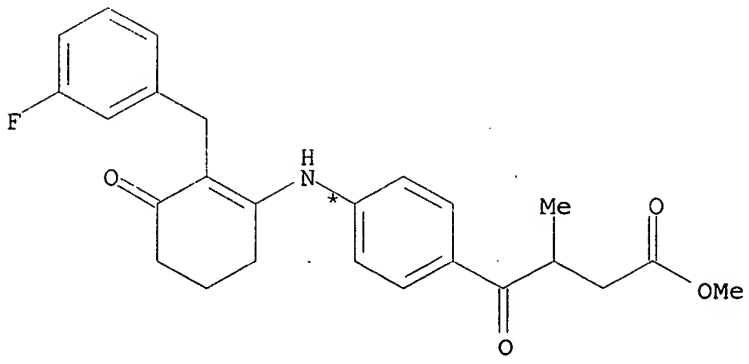


BE



CD

(27)

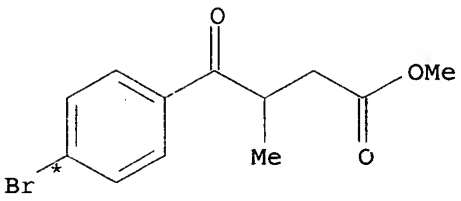


CE

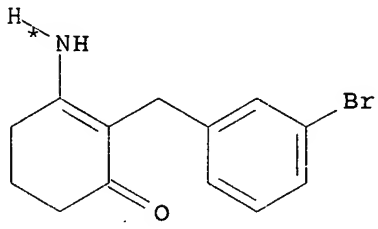
RX(27) RCT BE 150424-74-1, CD 644984-88-3
RGT E 534-17-8 Cs2CO3

PRO CE 644984-97-4
CAT 51364-51-3 Ph2-pentadienone Pd, 213697-53-1 [1,1'-Biphenyl]-2-amine, 2'-(dicyclohexylphosphino)-N,N-dimethyl-
SOL 109-99-9 THF
NTE Buchwald reaction

RX(28) OF 205 ...BE + CF ===> CG...

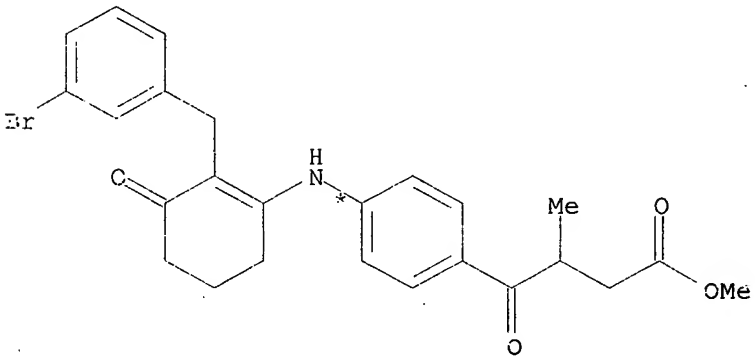


BE



CF

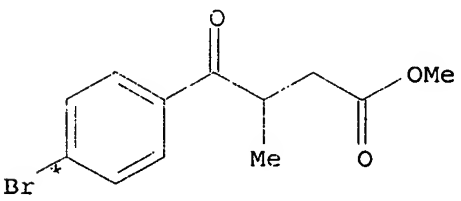
(28)



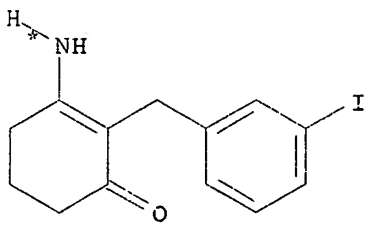
CG

RX(28) RCT BE 150424-74-1, CF 644984-89-4
RGT E 534-17-8 Cs2CO3
PRO CG 644984-98-5
CAT 51364-51-3 Ph2-pentadienone Pd, 213697-53-1 [1,1'-Biphenyl]-2-amine, 2'-(dicyclohexylphosphino)-N,N-dimethyl-
SOL 109-99-9 THF
NTE Buchwald reaction

RX(29) OF 205 ...BE + CH ===> CI...

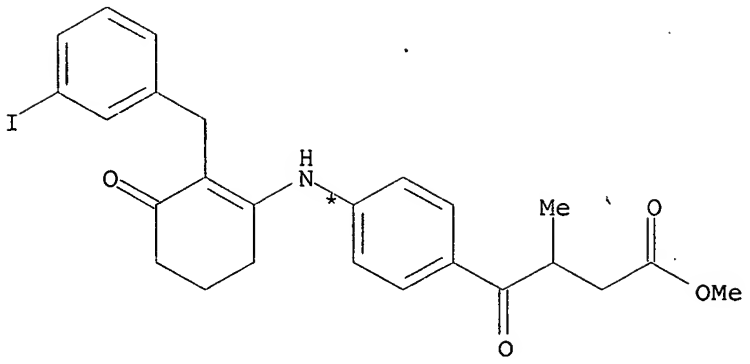


BE



CH

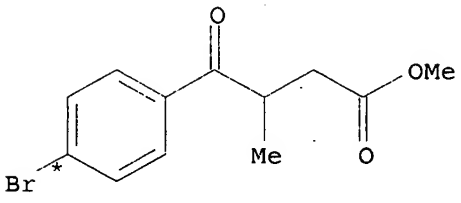
(29)



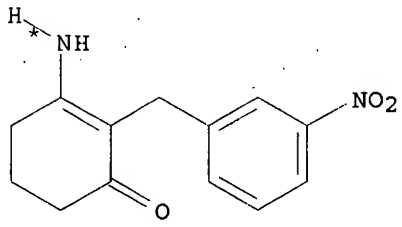
CI

RX(29) RCT BE 150424-74-1, CH 644984-90-7
RGT E 534-17-8 Cs2CO3
PRO CI 644984-99-6
CAT 51364-51-3 Ph2-pentadienone Pd, 213697-53-1 [1,1'-Biphenyl]-2-amine, 2'-(dicyclohexylphosphino)-N,N-dimethyl-
SOL 109-99-9 THF
NTE Buchwald reaction

RX(30) CF 205 ...BE + CJ ===> CK...

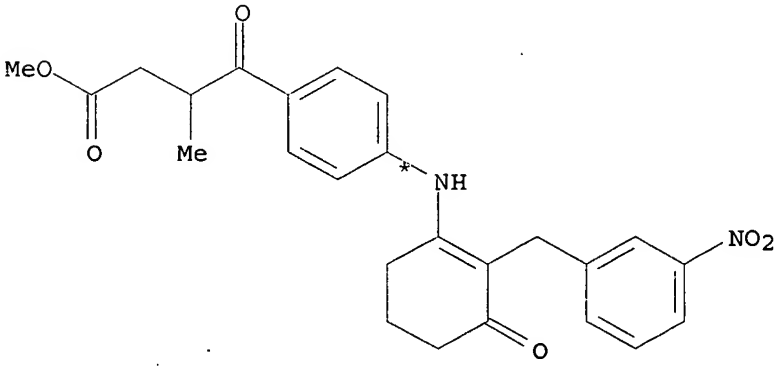


BE



CJ

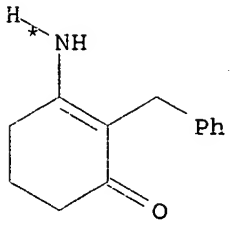
(30)



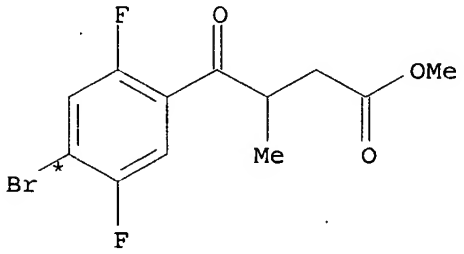
CK

RX(30) RCT BE 150424-74-1, CJ 644984-91-8
RGT E 534-17-8 Cs2CO3
PRO CK 644985-00-2
CAT 51364-51-3 Ph2-pentadienone Pd, 213697-53-1 [1,1'-Biphenyl]-2-amine, 2'-(dicyclohexylphosphino)-N,N-dimethyl-
SOL 109-99-9 THF
NTE Buchwald reaction

RX(31) OF 205 ...CL + BX ===> CM...

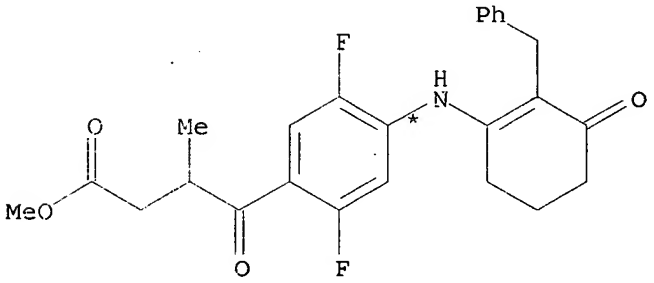


CL



BX

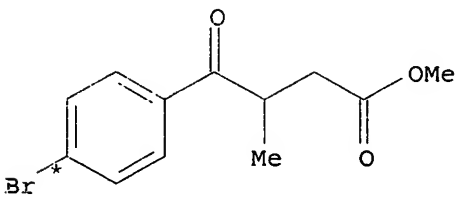
(31) →



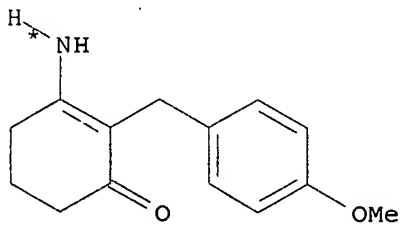
CM

RX(31) RCT CL 266306-27-8, BX 644984-85-0
RGT E 534-17-8 Cs2CO3
PRO CM 644985-01-3
CAT 51364-51-3 Ph2-pentadienone Pd, 213697-53-1 [1,1'-Biphenyl]-2-amine, 2'-(dicyclohexylphosphino)-N,N-dimethyl-
SOL 109-99-9 THF
NTE Buchwald reaction

RX(32) OF 205 ...BE + CN ===> CO...

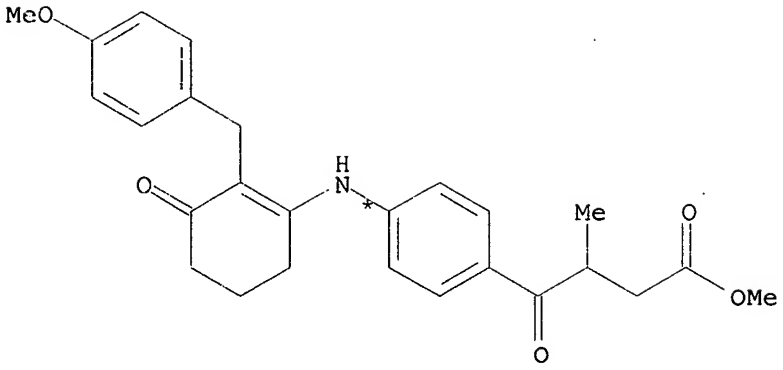


BE



CN

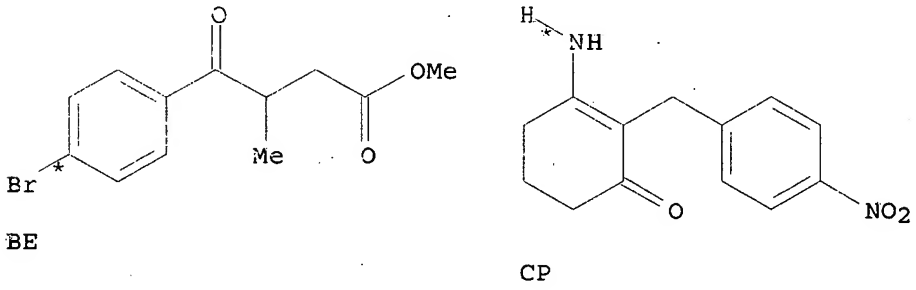
(32) →



CC

RX(32) RCT BE 150424-74-1, CN 644984-93-0
RGT E 534-17-8 Cs2CO3
PRO CO 644985-02-4
CAT 51364-51-3 Ph2-pentadienone Pd, 213697-53-1 [1,1'-Biphenyl]-2-amine, 2'-(dicyclohexylphosphino)-N,N-dimethyl-
SOL 109-99-9 THF
NTE Buchwald reaction

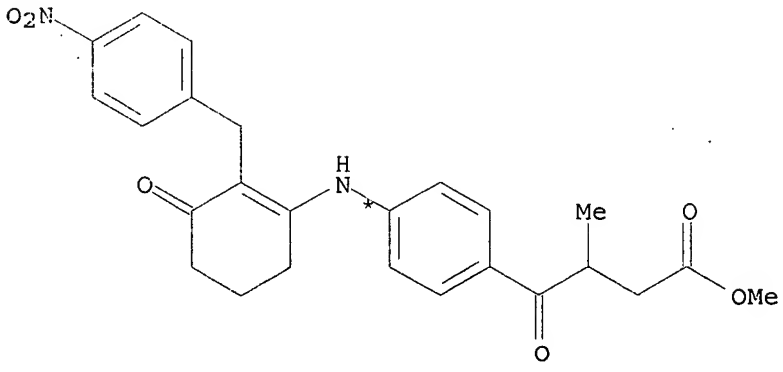
RX(33) OF 205 ...BE + CP ===> CQ...



BE

CP

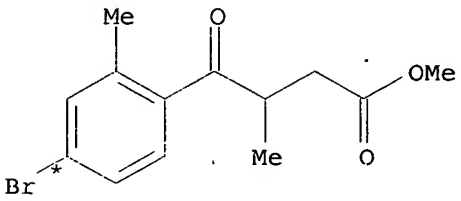
(33)



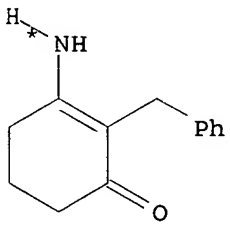
CQ

RX(33) RCT BE 150424-74-1, CP 644984-94-1
RGT E 534-17-8 Cs2CO3
PRO CQ 644985-03-5
CAT 51364-51-3 Ph2-pentadienone Pd, 213697-53-1 [1,1'-Biphenyl]-2-amine, 2'-(dicyclohexylphosphino)-N,N-dimethyl-
SOL 109-99-9 THF
NTE Buchwald reaction

RX(34) OF 205 ...BL + CL ===> CR...

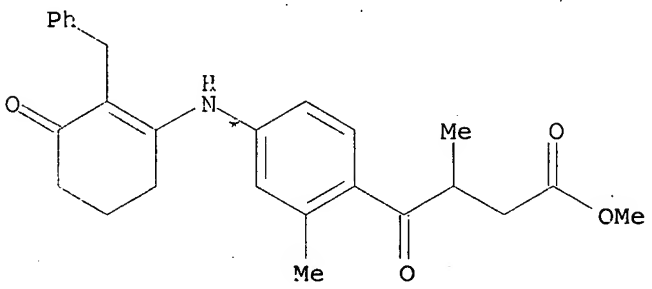


BL



CL

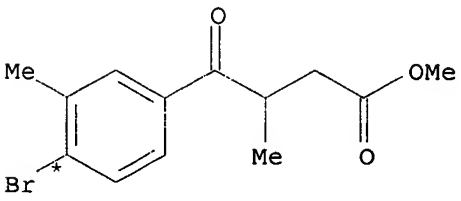
(34) ⟶



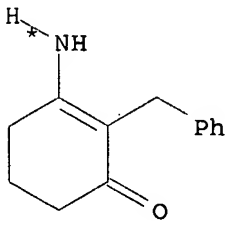
CR

RX(34) RCT BL 644984-79-2, CL 266306-27-8
RGT E 534-17-8 Cs2CO3
PRO CR 644985-04-6
CAT 51364-51-3 Ph2-pentadienone Pd, 213697-53-1 [1,1'-Biphenyl]-2-amine, 2'-(dicyclohexylphosphino)-N,N-dimethyl-
SOL 109-99-9 THF
NTE Buchwald reaction

RX(35) OF 205 ...BN + CL ===> CS...

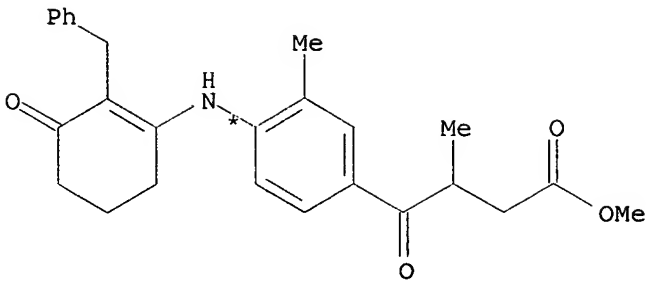


BN



CL

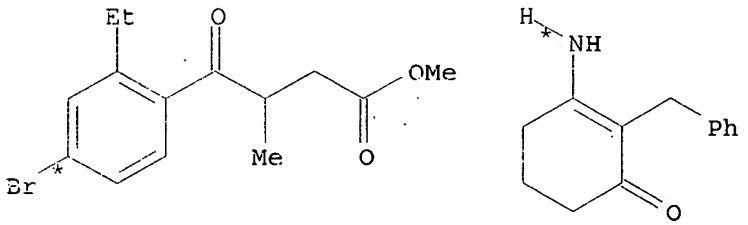
(35) ⟶



CS

RX(35) RCT BN 644984-80-5, CL 266306-27-8
RGT E 534-17-8 Cs2CO3
PRO CS 644985-05-7
CAT 51364-51-3 Ph2-pentadienone Pd, 213697-53-1 [1,1'-Biphenyl]-2-amine, 2'-(dicyclohexylphosphino)-N,N-dimethyl-
SOL 109-99-9 THF
NTE Buchwald reaction

RX(36) OF 205 ...BP + CL ===> CT...

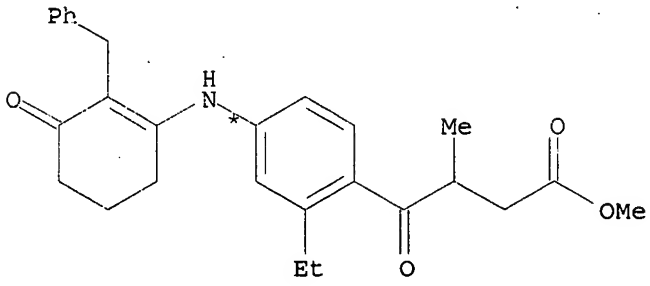


BP



CL

(36)

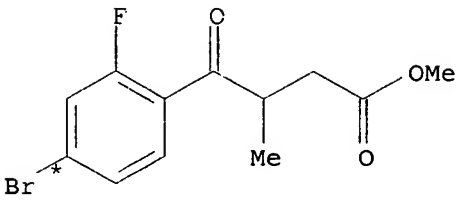


CT

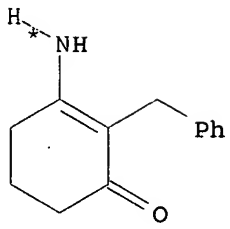
RX(36) RCT BP 644984-81-6, CL 266306-27-8
RGT E 534-17-8 Cs2CO3
PRO CT 644985-06-8
CAT 51364-51-3 Ph2-pentadienone Pd, 213697-53-1 [1,1'-Biphenyl]-2-amine, 2'-(dicyclohexylphosphino)-N,N-dimethyl-
SOL 109-99-9 THF

NTE Buchwald reaction

RX(37) OF 205 ...BR + CL ===> CU...

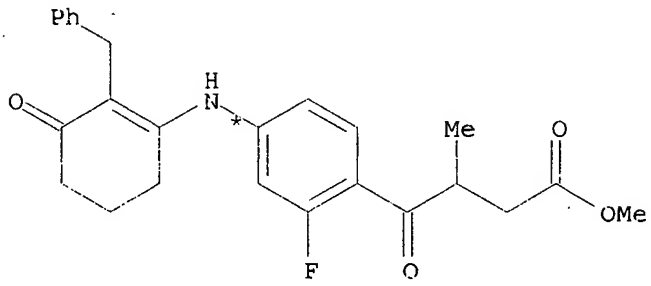


BR



CL

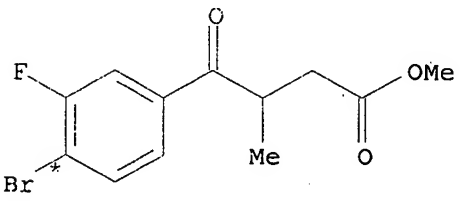
(37)



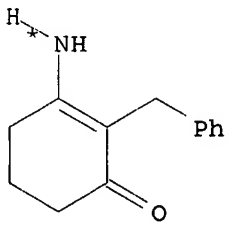
CU

RX(37) RCT BR 644984-82-7, CL 266306-27-8
RGT E 534-17-8 Cs2CO3
PRO CU 644985-07-9
CAT 51364-51-3 Ph2-pentadienone Pd, 213697-53-1 [1,1'-Biphenyl]-2-amine, 2'-(dicyclohexylphosphino)-N,N-dimethyl-
SOL 109-99-9 THF
NTE Buchwald reaction

RX(38) OF 205 ...BT + CL ===> CV...

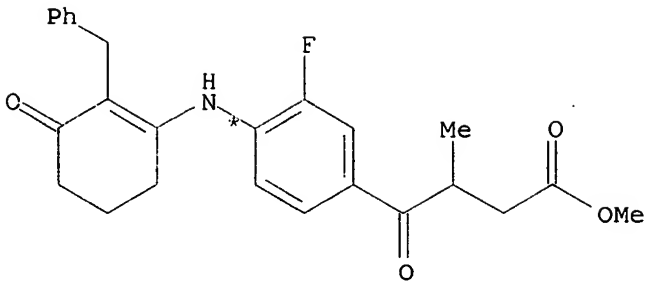


BT



CL

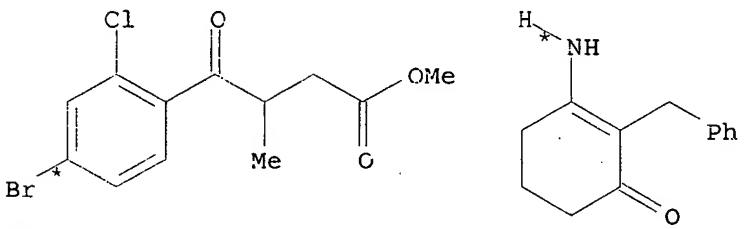
(38)



CV

RX(38) RCT BT 644984-83-8, CL 266306-27-8
RGT E 534-17-8 Cs2CO3
PRO CV 644985-08-0
CAT 51364-51-3 Ph2-pentadienone Pd, 213697-53-1 [1,1'-Biphenyl]-2-amine, 2'-(dicyclohexylphosphino)-N,N-dimethyl-
SOL 109-99-9 THF
NTE Buchwald reaction

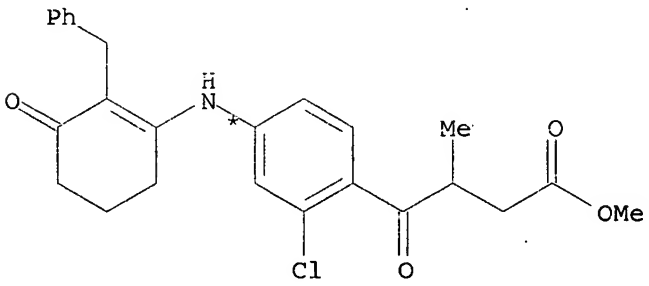
RX(39) OF 205 ...BV + CL ===> CW...



BV

CL

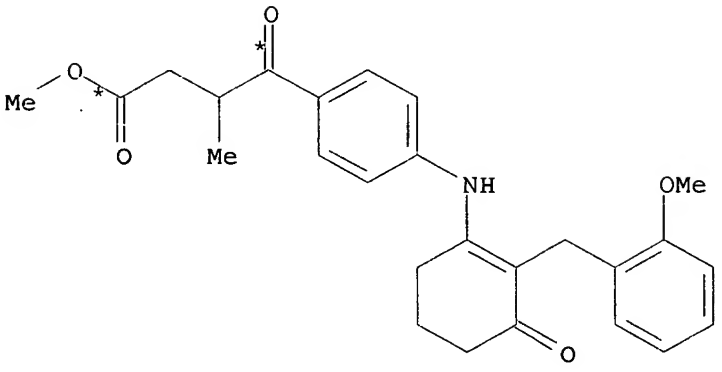
(39)



CW

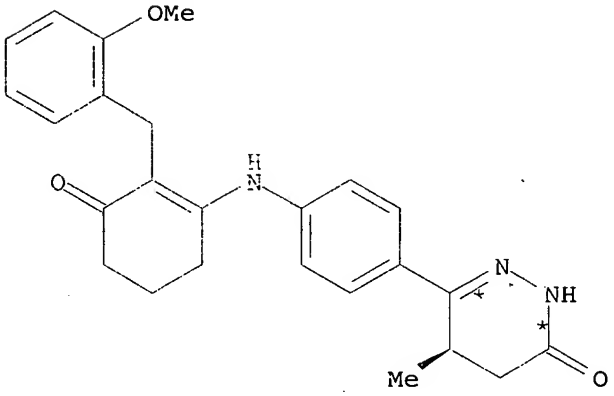
RX(39) RCT BV 644984-84-9, CL 266306-27-8
RGT E 534-17-8 Cs2CO3
PRO CW 644985-09-1
CAT 51364-51-3 Ph2-pentadienone Pd, 213697-53-1 [1,1'-Biphenyl]-2-amine, 2'-(dicyclohexylphosphino)-N,N-dimethyl-
SOL 109-99-9 THF
NTE Buchwald reaction

RX(40) OF 205 ...BZ ===> CX




BZ

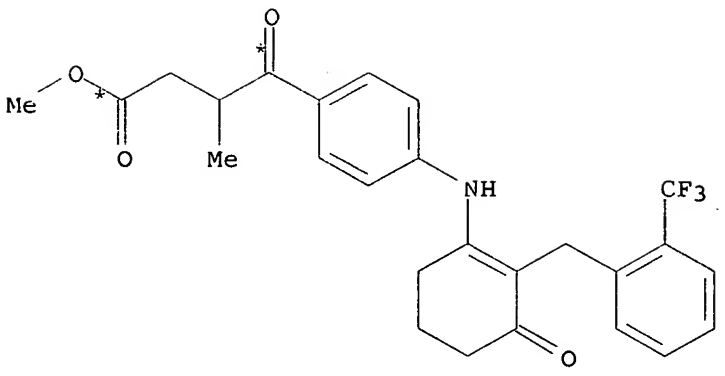
(40)




CX

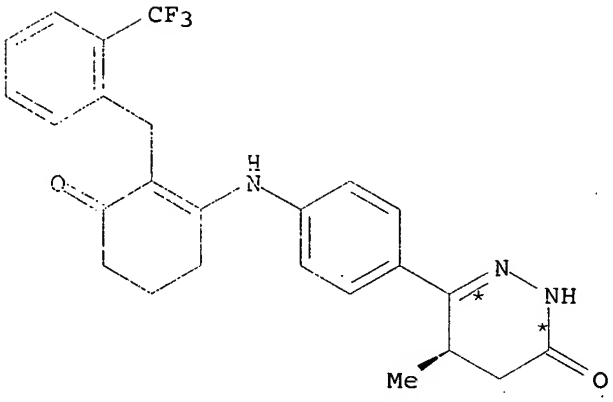
RX(40) RCT BZ 644984-95-2
RGT F 302-01-2 N2H4
PRO CX 644985-10-4
SOL 7732-18-5 Water, 67-56-1 MeOH

RX(41) OF 205 ...CC ===> CZ



CC

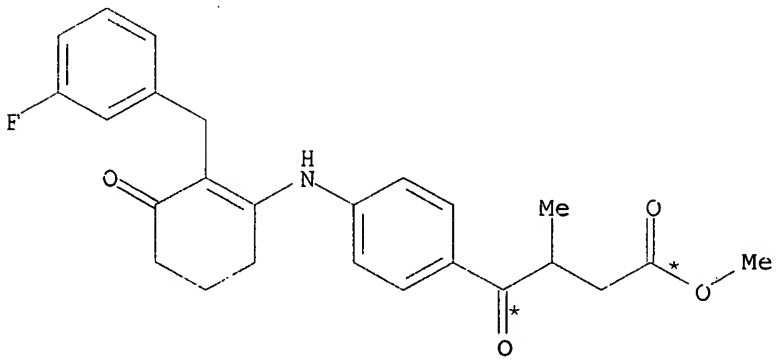
(41)



CZ

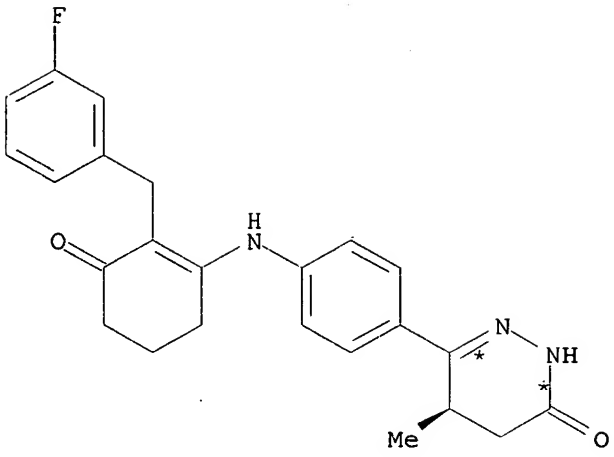
RX(41) RCT CC 644984-96-3
RGT F 302-01-2 N2H4
PRO CZ 644985-11-5
SOL 7732-18-5 Water, 67-56-1 MeOH

RX(42) OF 205 ...CE ===> DA



CE

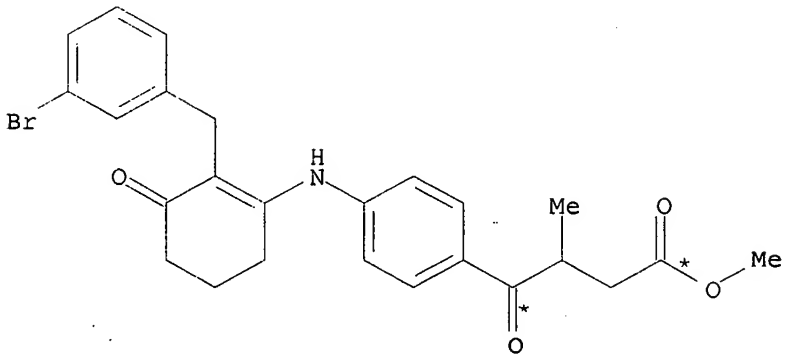
(42)



DA

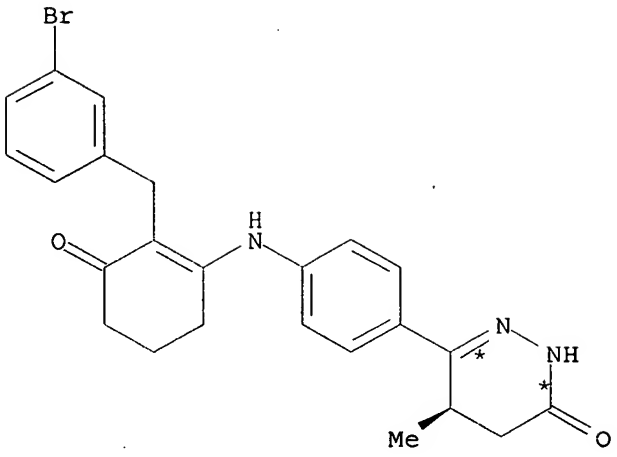
RX(42) RCT CE 644984-97-4
RGT F 302-01-2 N2H4
PRO DA 644985-12-6
SOL 7732-18-5 Water, 67-56-1 MeOH

RX(43) OF 205 ...CG ===> DB



CG

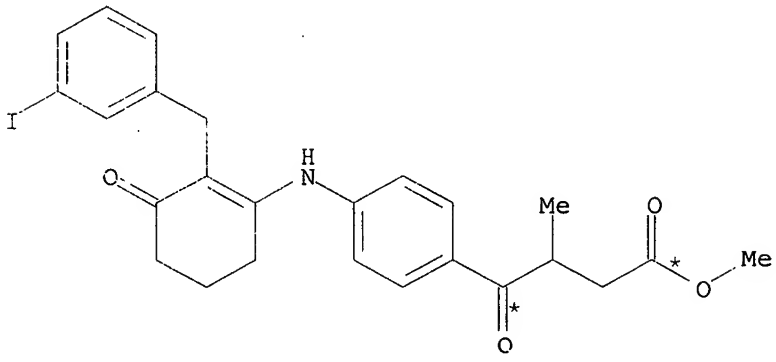
(43)




DB

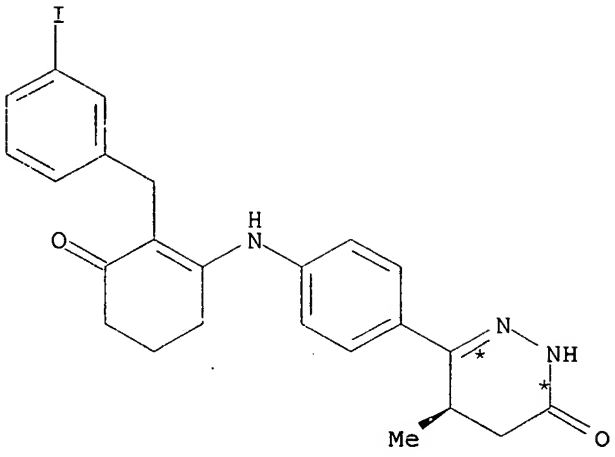
RX(43) RCT CG 644984-98-5
RGT F 302-01-2 N2H4
PRO DB 644984-67-8
SOL 7732-18-5 Water, 67-56-1 MeOH

RX(44) OF 205 ...CI ===> DC




CI

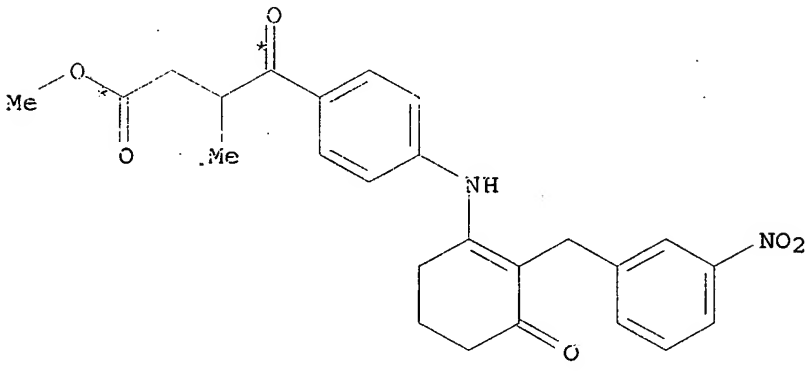
(44)



DC

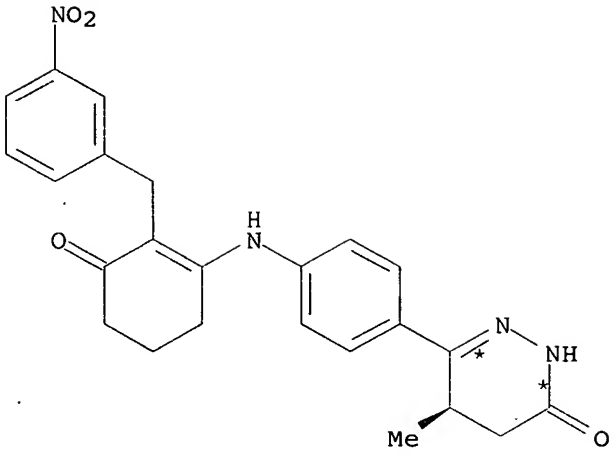
RX(44) RCT CI 644984-99-6
RGT F 302-01-2 N2H4
PRO DC 644985-13-7
SOL 7732-18-5 Water, 67-56-1 MeOH

RX(45) OF 205 ...CK ===> DD



CK

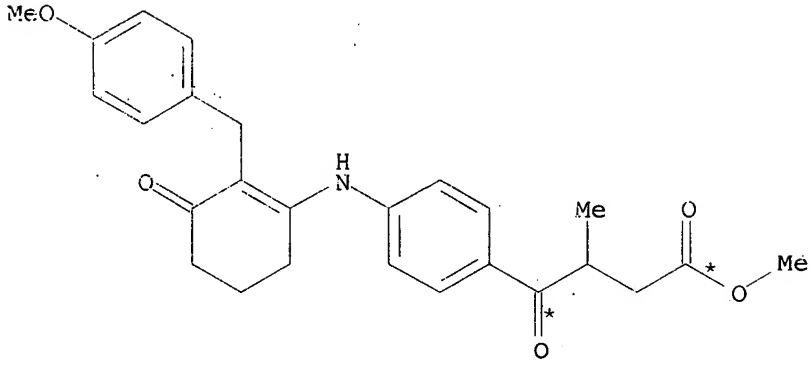
(45)



DD

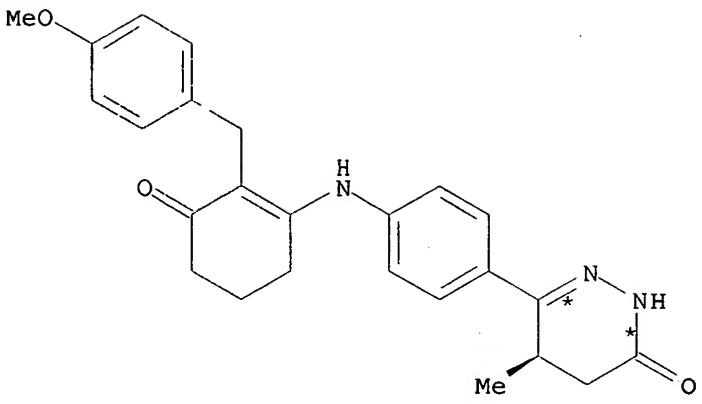
RX(45) RCT CK 644985-00-2
RGT F 302-01-2 N2H4
PRO DD 644985-14-8
SOL 7732-18-5 Water, 67-56-1 MeOH

RX(46) OF 205 ...CO ===> DE



CO

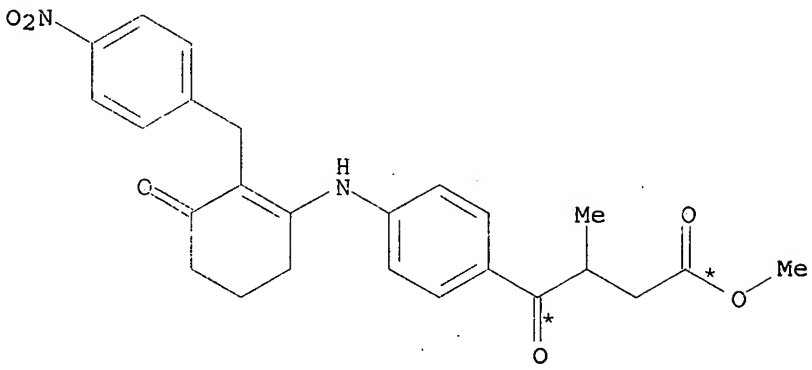
(46)



DE

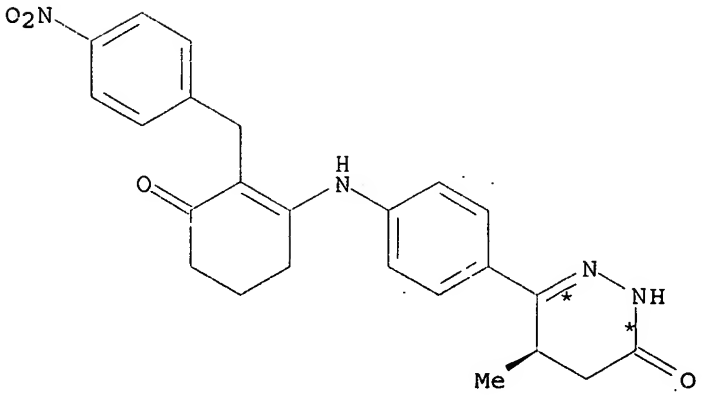
RX(46) RCT CO 644985-02-4
RGT F 302-01-2 N2H4
PRO DE 644985-15-9
SOL 7732-18-5 Water, 67-56-1 MeOH

RX(47) OF 205 ...CQ ===> DF



CQ

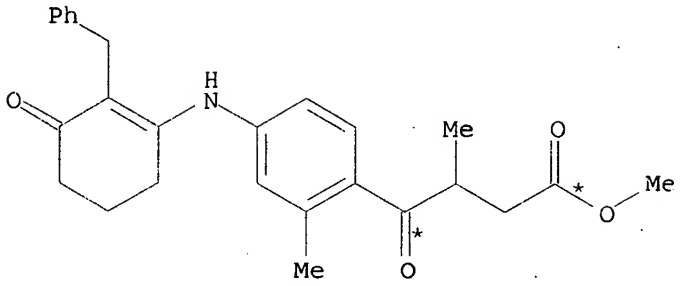
(47)



DF

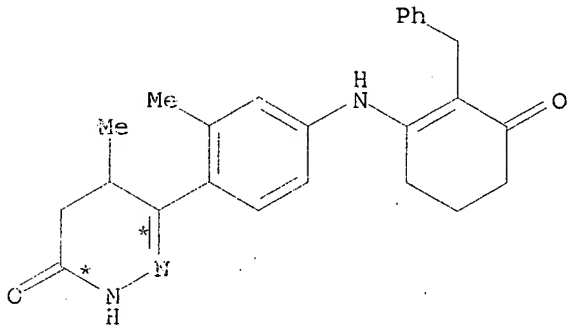
RX(47) RCT CQ 644985-03-5
RGT F 302-01-2 N2H4
PRO DF 644985-16-0
SOL 7732-18-5 Water, 67-56-1 MeOH

RX(48) OF 205 ...CR ===> DG



CR

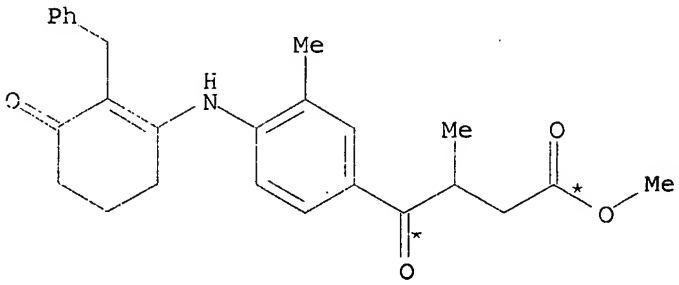
(48)



DG

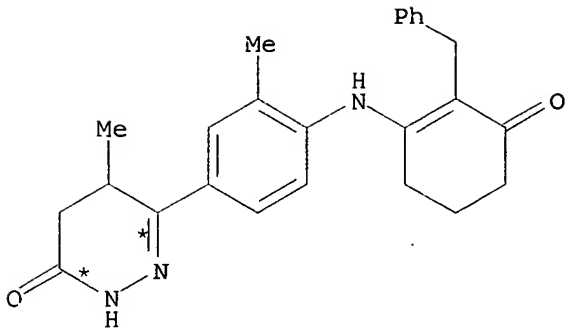
RX(48) RCT CR 644985-04-6
RGT F 302-01-2 N2H4
PRO DG 644985-17-1
SOL 7732-18-5 Water, 67-56-1 MeOH

RX(49) OF 205 ...CS ===> DH



CS

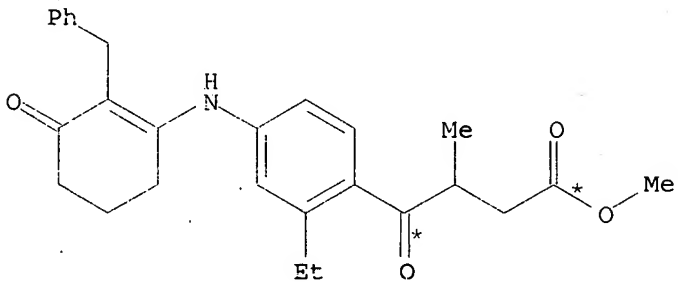
(49)



DH

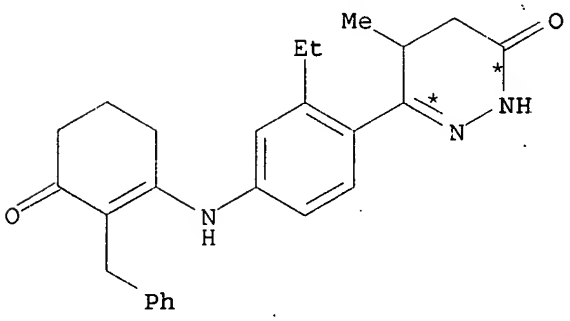
RX(49) RCT CS 644985-05-7
RGT F 302-01-2 N2H4
PRO DH 644985-18-2
SOL 7732-18-5 Water, 67-56-1 MeOH

RX(50) OF 205 ...CT ===> DI



CT

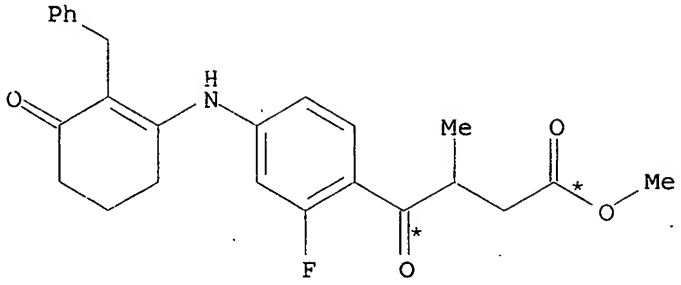
(50)



DI

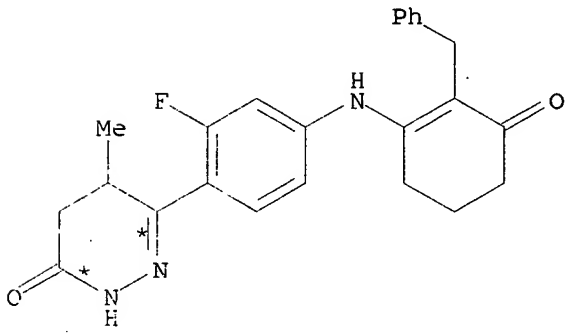
RX(50) RCT CT 644985-06-8
RGT F 302-01-2 N2H4
PRO DI 644985-19-3
SOL 7732-18-5 Water, 67-56-1 MeOH

RX(51) OF 205 ...CU ===> DJ



CU

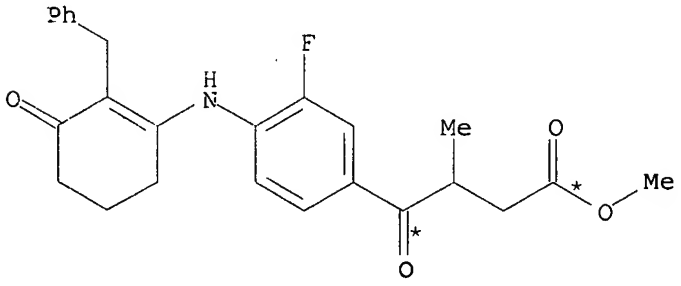
(51)



DJ

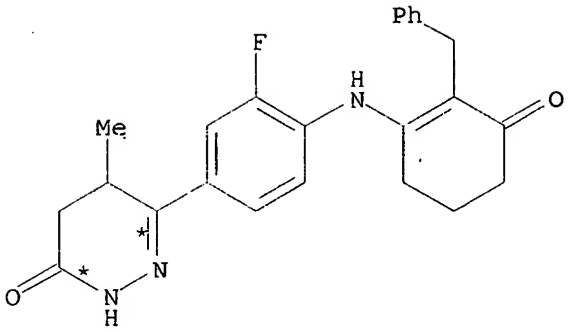
RX(51) RCT CU 644985-07-9
RGT F 302-01-2 N2H4
PRO DJ 644985-20-6
SOL 7732-18-5 Water, 67-56-1 MeOH

RX(52) OF 205 ...CV ===> DK



CV

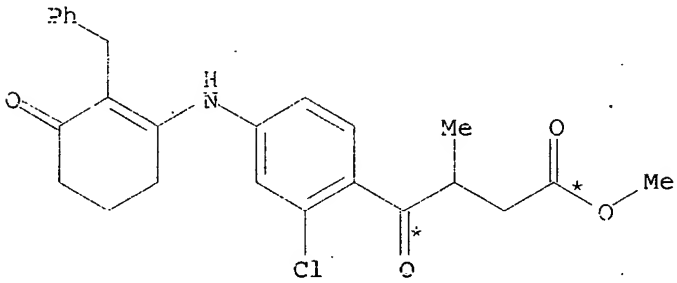
(52)




DK

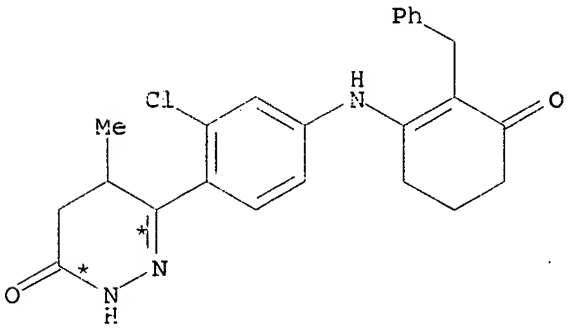
RX(52) RCT CV 644985-08-0
RGT F 302-01-2 N2H4
PRO DK 644985-21-7
SOL 7732-18-5 Water, 67-56-1 MeOH

RX(53) OF 205 ...CW ===> DL




CW

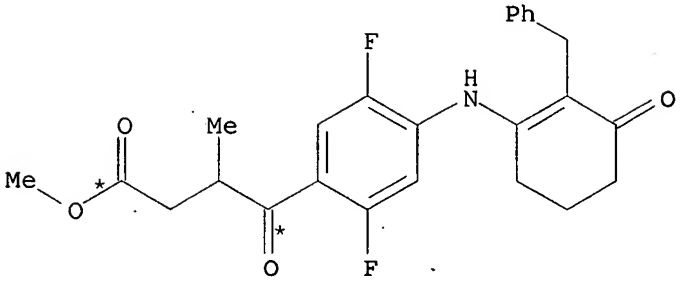
(53) ⟶




DL

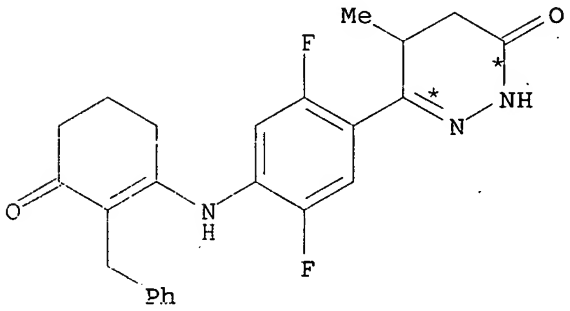
RX(53) RCT CW 644985-09-1
RGT F 302-01-2 N2H4
PRO DL 644985-22-8
SOL 7732-18-5 Water, 67-56-1 MeOH

RX(54) OF 205 ...CM ===> DM



CM

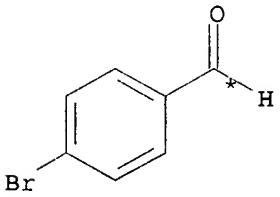
(54)



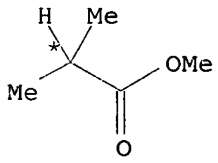
DM

RX(54) RCT CM 644985-01-3
RGT F 302-01-2 N2H4
PRO DM 644985-23-9
SOL 7732-18-5 Water, 67-56-1 MeOH

RX(55) OF 205 DN + DO ===> DP...

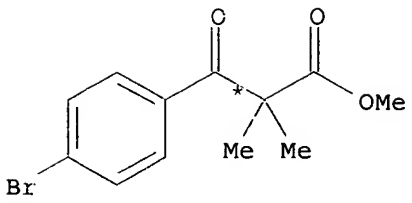


DN



DO

(55)



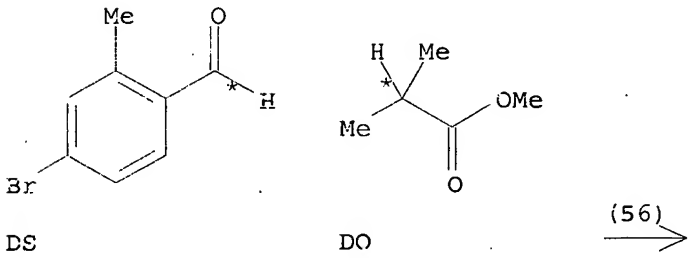
DP

RX(55)  RCT  DN 1122-91-4, DO 547-63-7

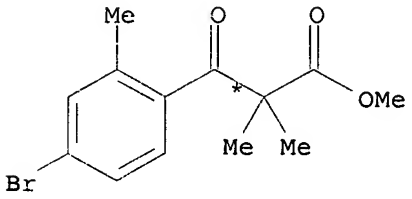
STAGE(1)
RGT  DQ 4111-54-0 LiN(Pr-i)2
SOL  109-99-9 THF

STAGE(2)
RGT  DR 87413-09-0 Martin's reagent
SOL  75-09-2 CH2Cl2
PRO  DP 644985-25-1

RX(56) OF 205  DS + DO ===> DT...



DS  DO  (56)



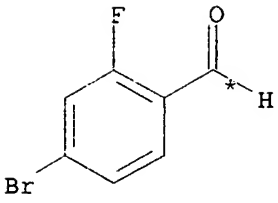
DT

RX(56)  RCT  DS 24078-12-4, DO 547-63-7

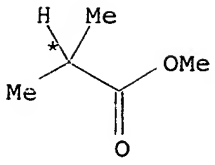
STAGE(1)
RGT  DQ 4111-54-0 LiN(Pr-i)2
SOL  109-99-9 THF

STAGE(2)
RGT  DR 87413-09-0 Martin's reagent
SOL  75-09-2 CH2Cl2
PRO  DT 644985-26-2

RX(57) OF 205  DU + DO ===> DV...

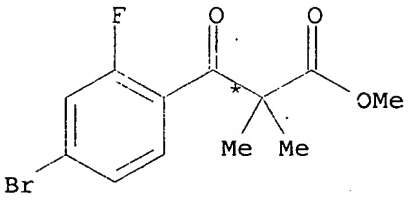


DU



DO

(57)



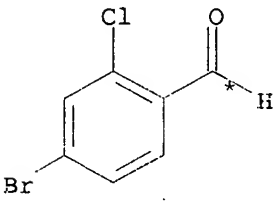
DV

RX(57) RCT DU 57848-46-1, DO 547-63-7

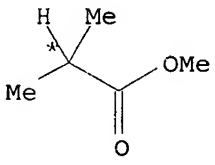
STAGE(1)
RGT DQ 4111-54-0 LiN(Pr-i)2
SOL 109-99-9 THF

STAGE(2)
RGT DR 87413-09-0 Martin's reagent
SOL 75-09-2 CH2Cl2
PRO DV 644985-27-3

RX(58) OF 205 DW + DO ===> DX...

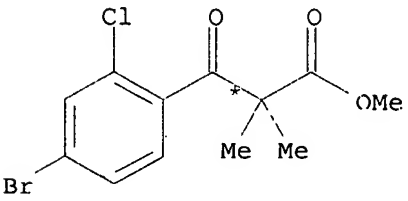


DW



DO

(58)



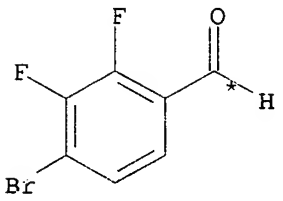
DX

RX(58)  RCT  DW 158435-41-7, DO 547-63-7

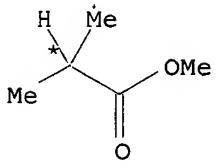
STAGE(1)
RGT  DQ 4111-54-0 LiN(Pr-i)2
SOL  109-99-9 THF

STAGE(2)
RGT  DR 87413-09-0 Martin's reagent
SOL  75-09-2 CH2Cl2
PRO  DX 644985-28-4

RX(59) OF 205  DY + DO ===> DZ...

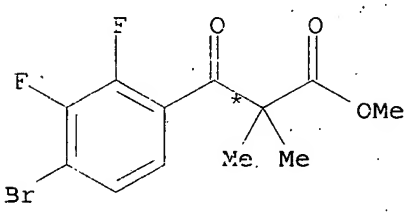


DY



DO

(59)



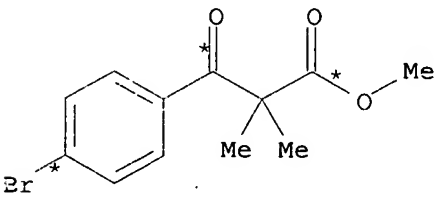
DZ

RX(59)  RCT  DY 644985-24-0, DO 547-63-7

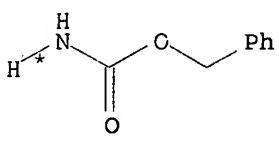
STAGE(1)
RGT  DQ 4111-54-0 LiN(Pr-i)2
SOL  109-99-9 THF

STAGE(2)
RGT  DR 87413-09-0 Martin's reagent
SOL  75-09-2 CH2Cl2
PRO  DZ 644985-29-5

RX(60) OF 205  ...DP + D ===> EA...

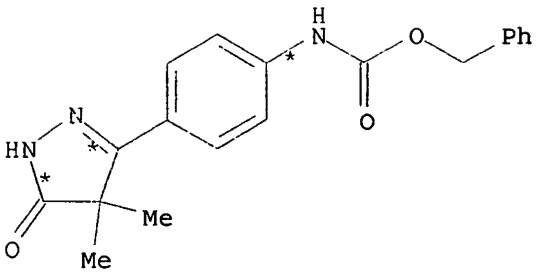


DP



D

(60)



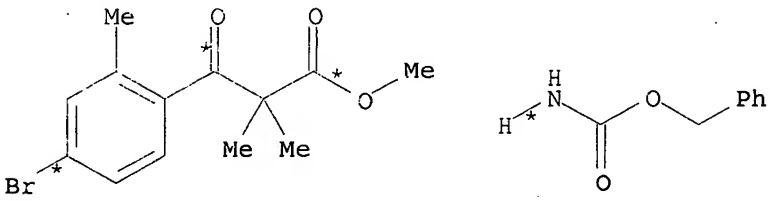
EA

RX(60)  RCT  DP 644985-25-1, D 621-84-1

STAGE(1)
RGT  E 534-17-8 Cs2CO3
CAT  51364-51-3 Ph2-pentadienone Pd, 161265-03-8 Phosphine, (9,9-dimethyl-9H-xanthene-4,5-diyl)bis[diphenyl-
SOL  109-99-9 THF

STAGE(2)
RGT  F 302-01-2 N2H4
SOL  64-17-5 EtOH
PRO  EA 644985-30-8
NTE  Buchwald reaction first stage

RX(61) OF 205  ...DT + D ===> EB...

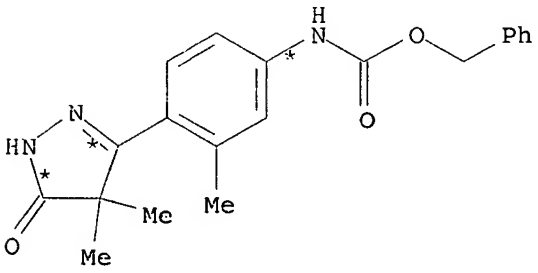


DT



D

(61)



EB

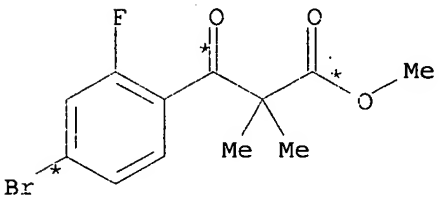
RX(61)  RCT  DT 644985-26-2, D 621-84-1

STAGE(1)

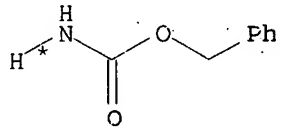
RGT E 534-17-8 Cs2CO3
CAT 51364-51-3 Ph2-pentadienone Pd, 161265-03-8 Phosphine, (9,9-dimethyl-9H-xanthene-4,5-diyl)bis[diphenyl-
SOL 109-99-9 THF

STAGE(2)
RGT F 302-01-2 N2H4
SOL 64-17-5 EtOH
PRO EB 644985-31-9
NTE Buchwald reaction first stage

RX(62) OF 205 ...DV + D ===> EC...

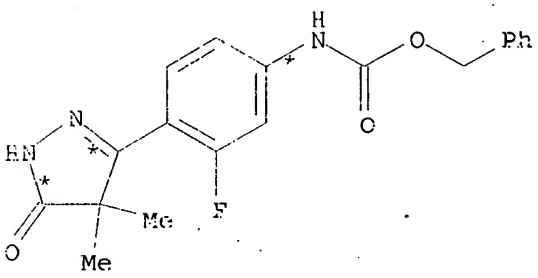


DV



D

(62)



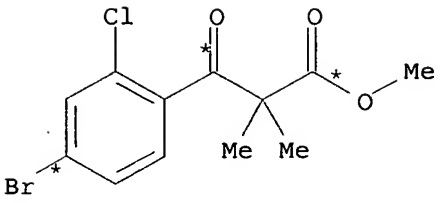
EC

RX(62) RCT DV 644985-27-3, D 621-84-1

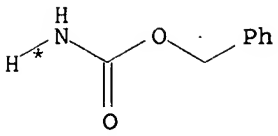
STAGE(1)
RGT E 534-17-8 Cs2CO3
CAT 51364-51-3 Ph2-pentadienone Pd, 161265-03-8 Phosphine, (9,9-dimethyl-9H-xanthene-4,5-diyl)bis[diphenyl-
SOL 109-99-9 THF

STAGE(2)
RGT F 302-01-2 N2H4
SOL 64-17-5 EtOH
PRO EC 644985-32-0
NTE Buchwald reaction first stage

RX(63) OF 205 ...DX + D ===> ED...

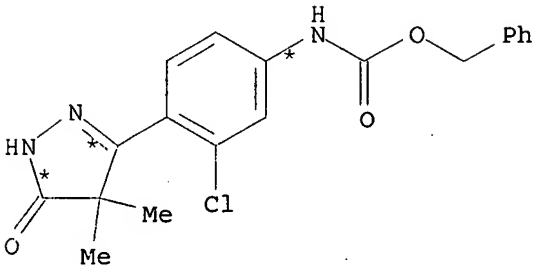


DX



D

(63)



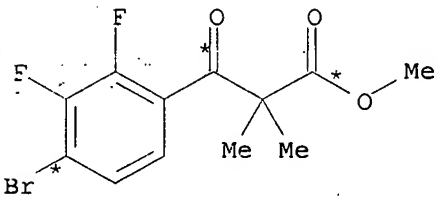
ED

RX(63) RCT DX 644985-28-4, D 621-84-1

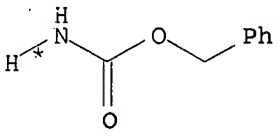
STAGE(1)
RGT E 534-17-8 Cs2CO3
CAT 51364-51-3 Ph2-pentadienone Pd, 161265-03-8 Phosphine, (9,9-dimethyl-9H-xanthene-4,5-diyl)bis[diphenyl-
SOL 109-99-9 THF

STAGE(2)
RGT F 302-01-2 N2H4
SOL 64-17-5 EtOH
PRO ED 644985-33-1
NTE Buchwald reaction first stage

RX(64) OF 205 ...DZ + D ===> EE...

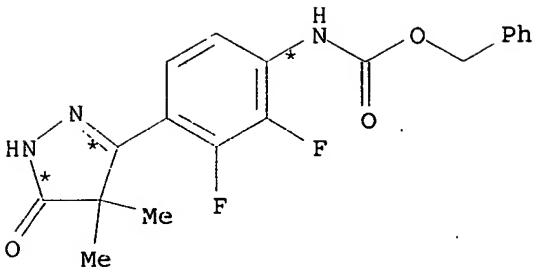


DZ



D

(64)



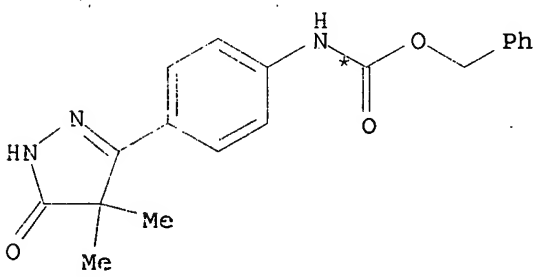
EE

RX(64) RCT DZ 644985-29-5, D 621-84-1

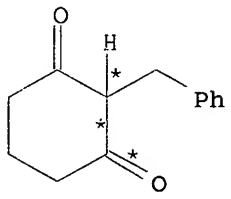
STAGE(1)
RGT E 534-17-8 Cs2CO3
CAT 51364-51-3 Ph2-pentadienone Pd, 161265-03-8 Phosphine, (9,9-dimethyl-9H-xanthene-4,5-diyl)bis[diphenyl-
SOL 109-99-9 THF

STAGE(2)
RGT F 302-01-2 N2H4
SOL 64-17-5 EtOH
PRO EE 644985-34-2
NTE Buchwald reaction first stage

RX(65) OF 205 ...**EA** + AO ===> **EF**

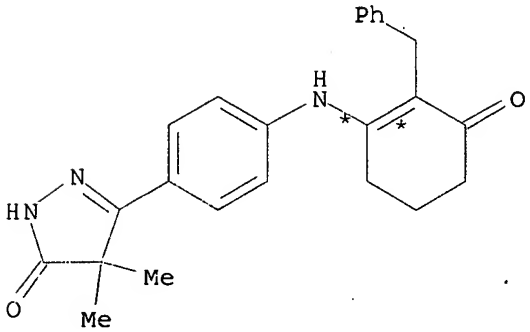


EA



AO

(65)



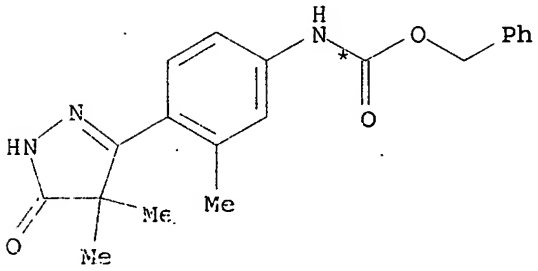
EF

RX(65)  RCT  EA **644985-30-8**

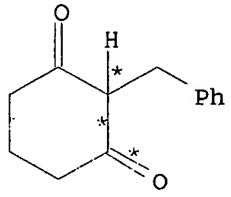
STAGE(1)
RGT  G 1333-74-0 H2
CAT  12135-22-7 Pd(OH)2
SOL  64-17-5 EtOH

STAGE(2)
RCT  AO 22381-56-2
CAT  104-15-4 TsOH
SOL  108-88-3 PhMe, 67-68-5 DMSO
PRO  EF **644985-35-3**
NTE  alternate prepn. also described

RX(66) OF 205  ...**EB** + AO ===> **EG**

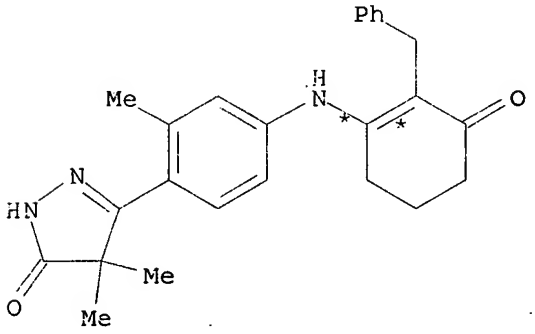


EB



AC

(66) ⟶



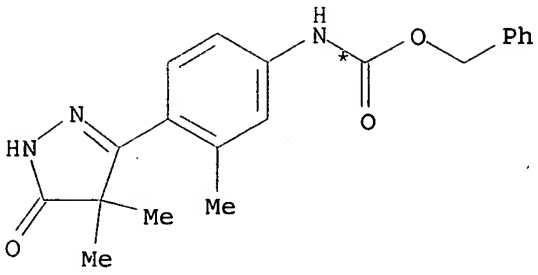
EG

RX(66)  RCT  EB **644985-31-9**

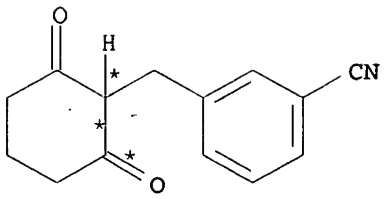
STAGE(1)
RGT  G 1333-74-0 H2
CAT  12135-22-7 Pd(OH)2
SOL  64-17-5 EtOH

STAGE(2)
RCT  AO 22381-56-2
CAT  104-15-4 TsOH
SOL  108-88-3 PhMe, 67-68-5 DMSO
PRO  EG **644985-36-4**
NTE  alternate prepn. also described

RX(67) OF 205 ...**EB** + B ===> **C**

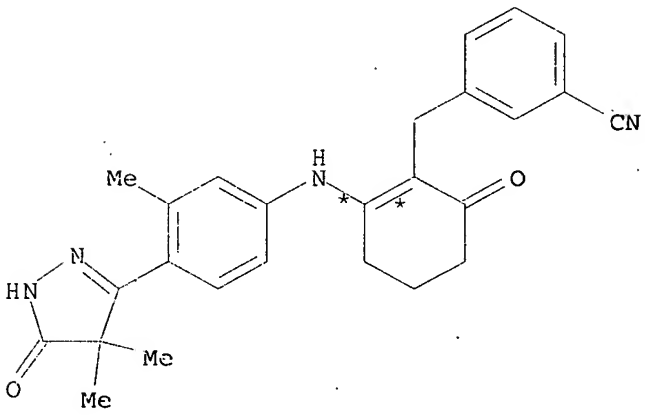


EB



B

(67)



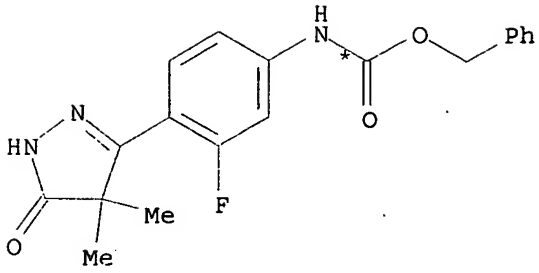
C

RX(67) RCT EB **644985-31-9**

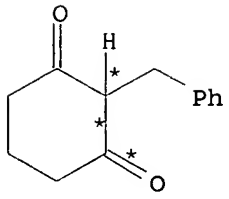
STAGE(1)
RGT G 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(2)
RCT B 724453-04-7
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe, 67-68-5 DMSO
PRO C **644985-37-5**
NTE alternate prepn. also described

RX(68) OF 205 ...**EC** + AO ===> **EH**

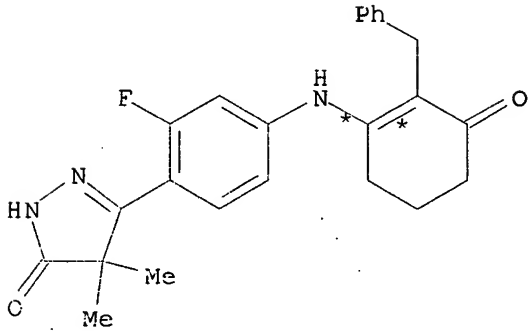


EC



AO

(68)



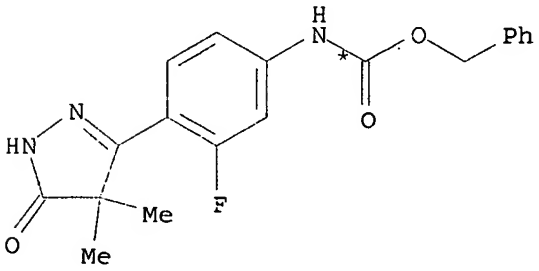
EH

RX(68) RCT EC **644985-32-0**

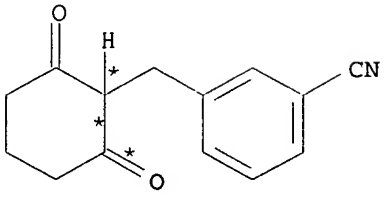
STAGE(1)
RGT G 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(2)
RCT AO 22381-56-2
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe, 67-68-5 DMSO
PRO EH **644985-38-6**
NTE alternate prepn. also described

RX(69) OF 205 ...**EC** + B ===> **Q**

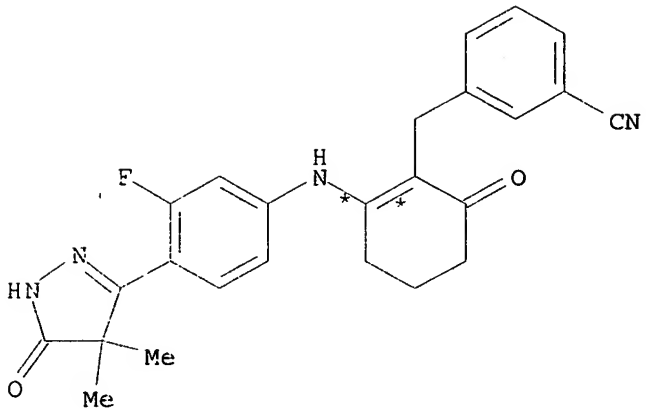


EC



B

(69)



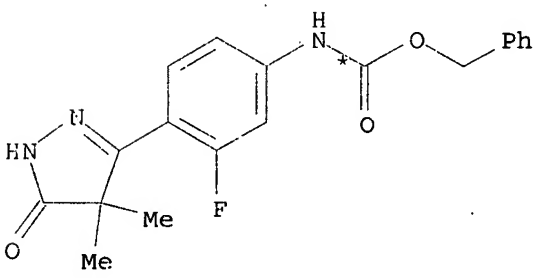
Q

RX(69) RCT EC **644985-32-0**

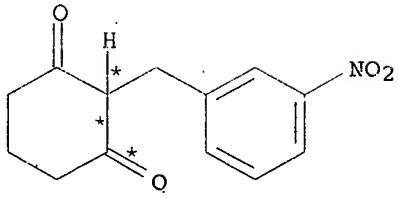
STAGE(1)
RGT G 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(2)
RCT B 724453-04-7
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe, 67-68-5 DMSO
PRO Q **644985-39-7**
NTE alternate prepn. also described

RX(70) OF 205 ...**EC** + R ===> **S**

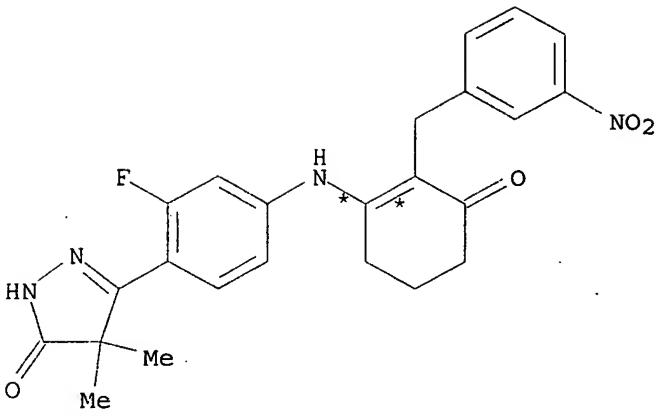


EC



R

(70)



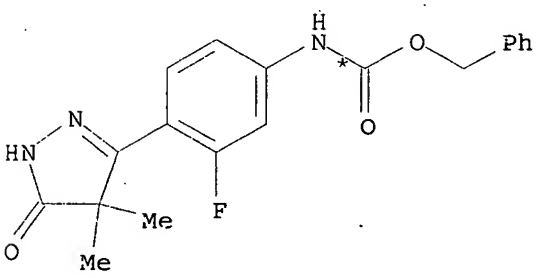
S

RX(70) RCT EC **644985-32-0**

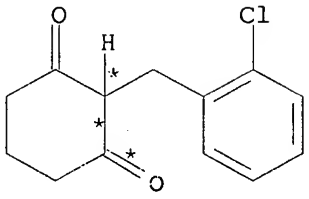
STAGE(1)
RGT G 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(2)
RCT R 724453-07-0
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe, 67-68-5 DMSO
PRO S **644985-40-0**
NTE alternate prepn. also described

RX(71) OF 205 ...**EC** + T ===> **U**

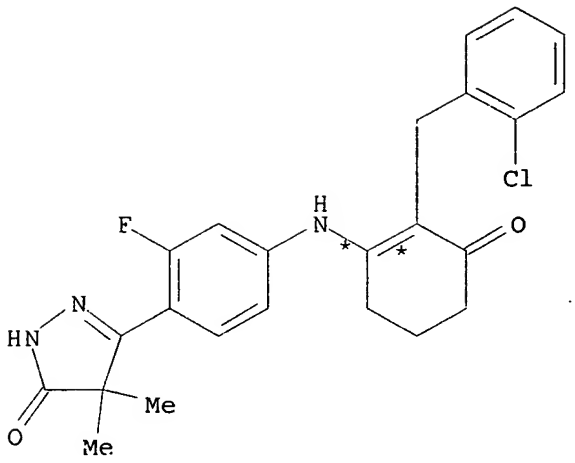


EC



T

(71)



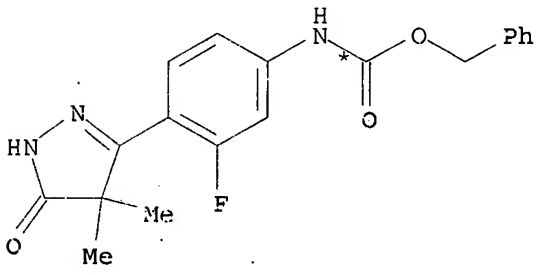
U

RX(71) RCT EC **644985-32-0**

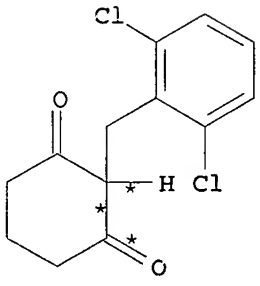
STAGE(1)
RGT G 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(2)
RCT T 724453-16-1
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe, 67-68-5 DMSO
PRO U **644985-41-1**
NTE alternate prepn. also described

RX(72) OF 205 ...**EC** + V ===> **W**

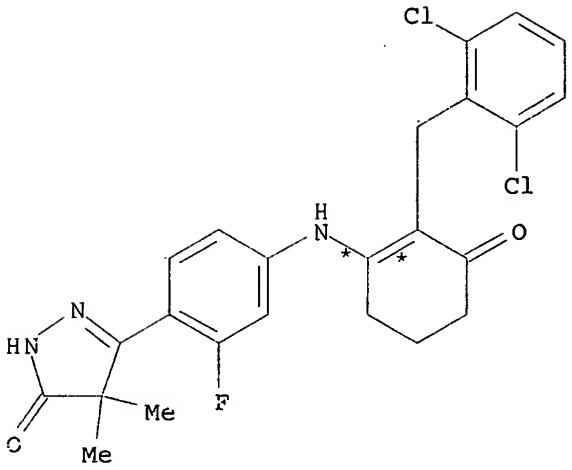


EC



V

(72)



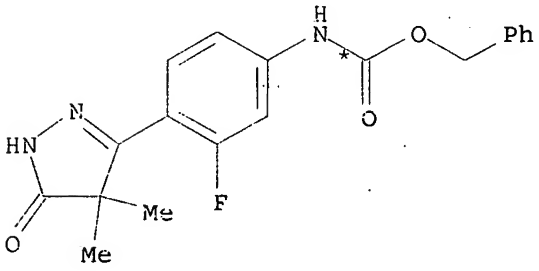
W

RX(72) RCT EC **644985-32-0**

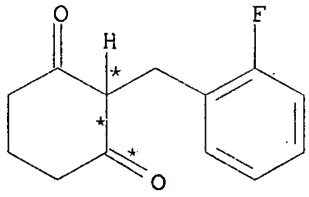
STAGE(1)
RGT G 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(2)
RCT V 724453-25-2
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe, 67-68-5 DMSO
PRO W **644985-42-2**
NTE alternate prepn. also described

RX(73) OF 205 ...**EC** + X ===> **Y**

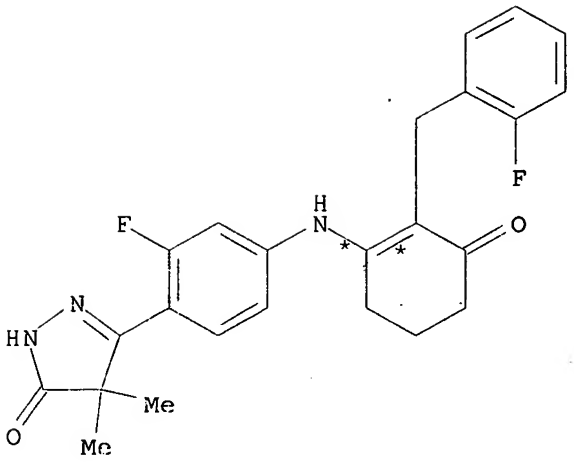


EC



X

(73)



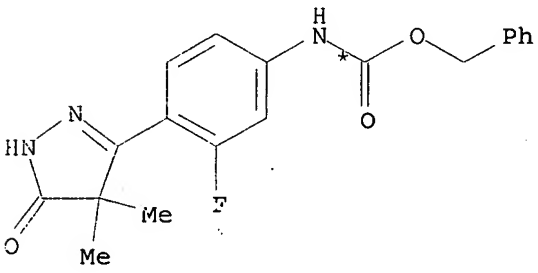
Y

RX(73) RCT EC **644985-32-0**

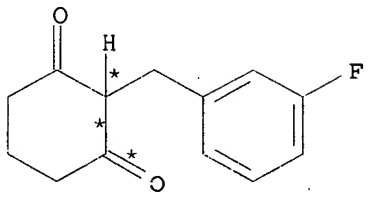
STAGE(1)
RGT G 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(2)
RCT X 724454-33-5
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe, 67-68-5 DMSO
PRC Y **644985-43-3**
NTE alternate prepn. also described

RX(74) OF 205 ...**EC** + Z ===> **AA**

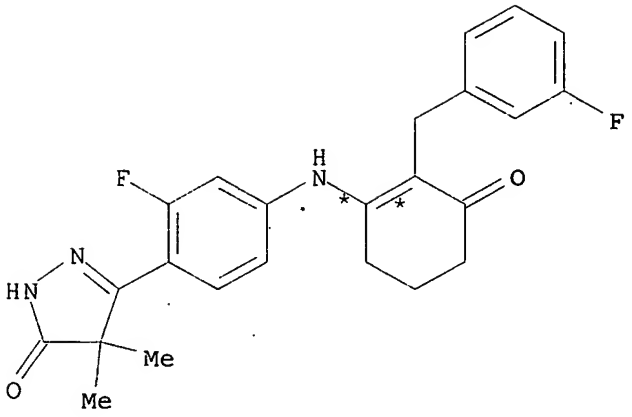


EC



Z

(74)



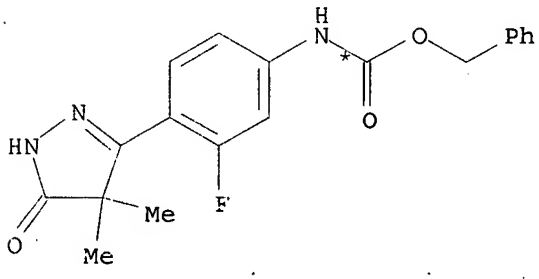
AA

RX(74) RCT EC **644985-32-0**

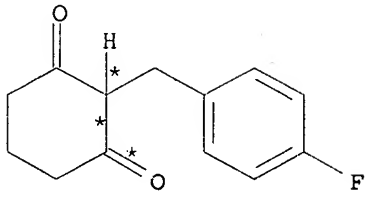
STAGE(1)
RGT G 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(2)
RCT Z 724455-21-4
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe, 67-68-5 DMSO
PRO AA **644985-44-4**
NTE alternate prepn. also described

RX(75) OF 205 ...**EC** + AB ===> **AC**

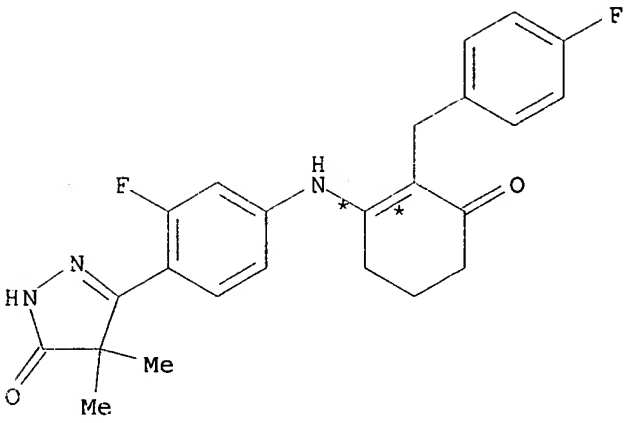


EC



AB

(75)



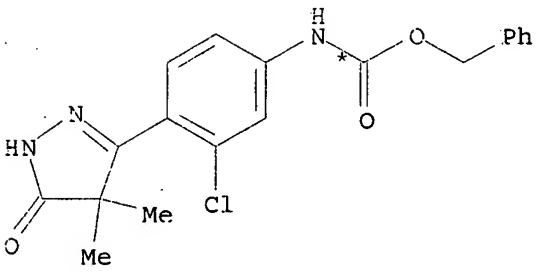
AC

RX(75) RCT EC **644985-32-0**

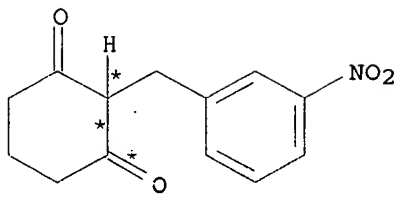
STAGE(1)
RGT G 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(2)
RCT AB 724456-36-4
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe, 67-68-5 DMSO
PRO AC **644985-45-5**
NTE alternate prepn. also described

RX(76) OF 205 ...**ED** + R ===> **EI**

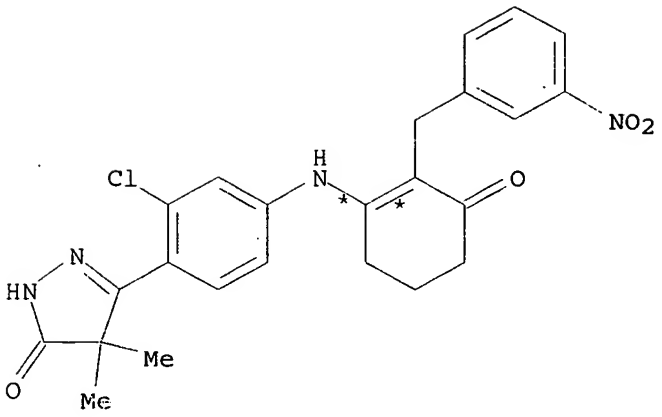


ED



R

(76)



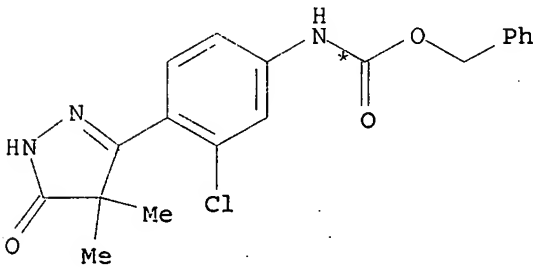
EI

RX(76) RCT ED **644985-33-1**

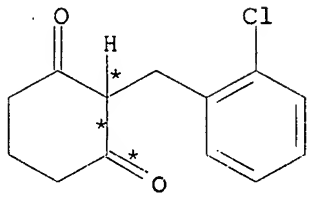
STAGE(1)
RGT G 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(2)
RCT R 724453-07-0
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe, 67-68-5 DMSO
PRO EI **644985-46-6**
NTE alternate prepn. also described

RX(77) OF 205 ...**ED** + T ===> **EJ**

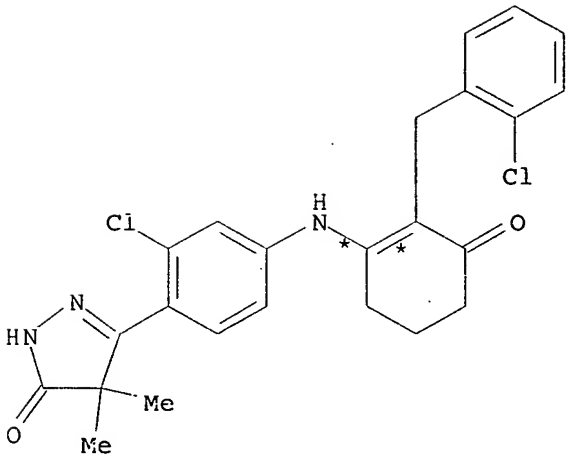


ED



T

(77)



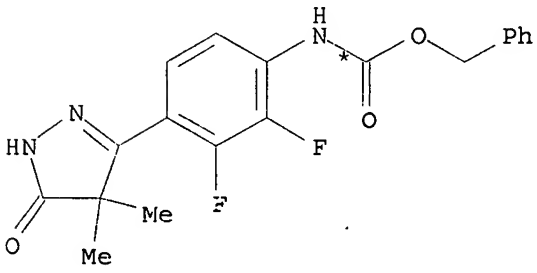
EJ

RX(77) RCT ED **644985-33-1**

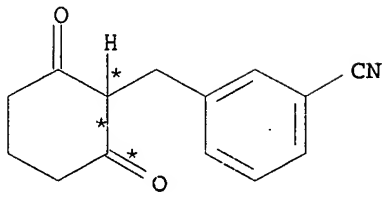
STAGE(1)
RGT G 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(2)
RCT T 724453-16-1
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe, 67-68-5 DMSO
PRO EJ **644985-47-7**
NTE alternate prepn. also described

RX(78) OF 205 ...**EE** + B ===> **EK**

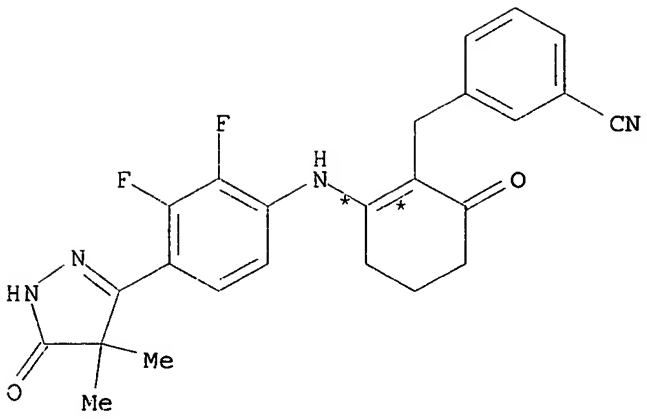


EE



B

(78)



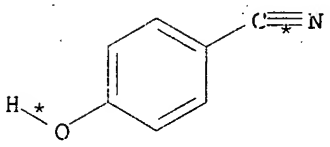
EK

RX(78) RCT EE **644985-34-2**

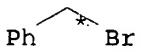
STAGE(1)
RGT G 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(2)
RCT B 724453-04-7
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe, 67-68-5 DMSO
PRO EK **644985-48-8**
NTE alternate prepn. also described

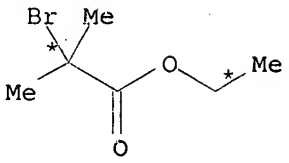
RX(79) OF 205 EL + EM + EN ===> EO...



EL

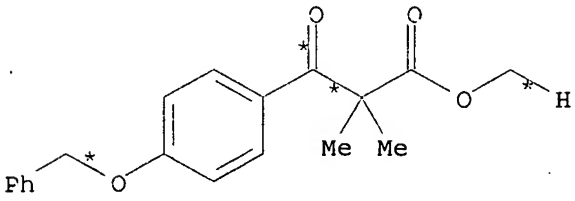


EM



EN

(79)

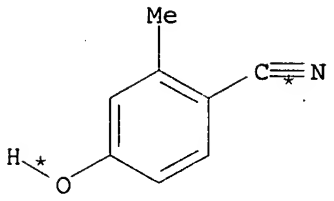


EO

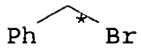
RX(79) RCT EL 767-00-0, EM 100-39-0, EN 600-00-0
RGT EP 7646-69-7 NaH
PRO EO 644985-49-9
CAT 311-28-4 Bu4N.I

SOL 109-99-9 THF

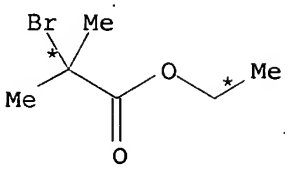
RX(80) OF 205 ER + EM + EN ===> ES...



ER

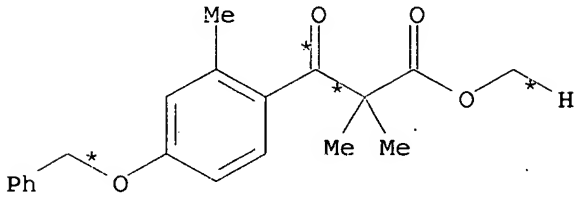


EM



EN

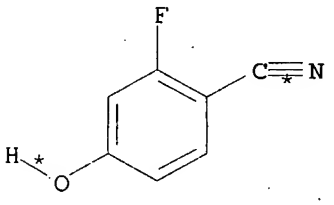
(80)



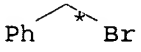
ES

RX(80) RCT ER 14143-26-1, EM 100-39-0, EN 600-00-0
RGT EP 7646-69-7 NaH
PRO ES 644985-50-2
CAT 311-28-4 Bu4N.I
SOL 109-99-9 THF

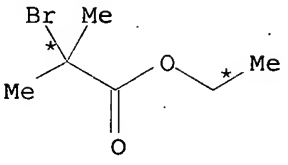
RX(81) OF 205 ET + EM + EN ===> EU...



ET

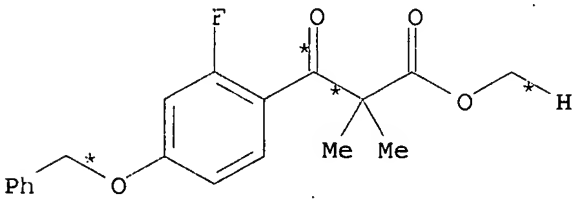


EM



EN

(81)

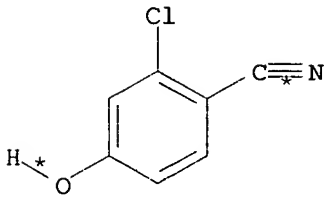


EU

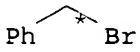
RX(81) RCT ET 82380-18-5, EM 100-39-0, EN 600-00-0
RGT EP 7646-69-7 NaH

PRO EU 644985-51-3
CAT 311-28-4 Bu4N.I
SOL 109-99-9 THF

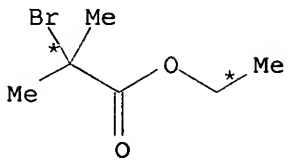
RX(82) OF 205 EV + EM + EN ===> EW...



EV

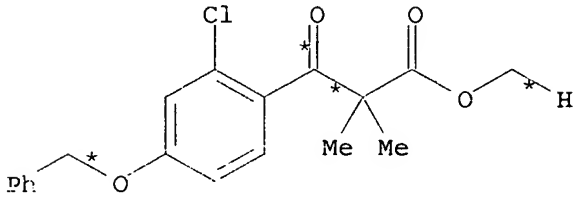


EM



EN

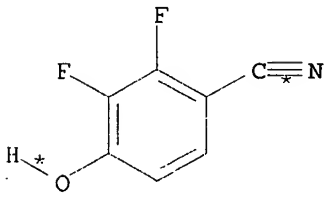
(82)



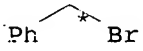
EW

RX(82) RCT EV 3336-16-1, EM 100-39-0, EN 600-00-0
RGT EP 7646-69-7 NaH
PRO EW 644985-52-4
CAT 311-28-4 Bu4N.I
SOL 109-99-9 THF

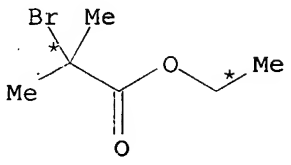
RX(83) OF 205 EX + EM + EN ===> EY...



EX

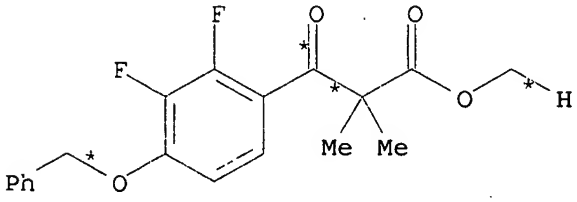


EM



EN

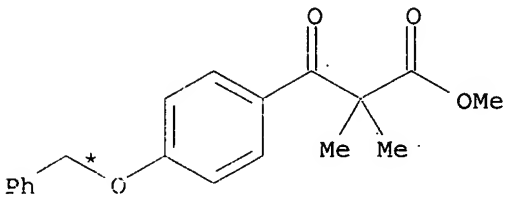
(83)



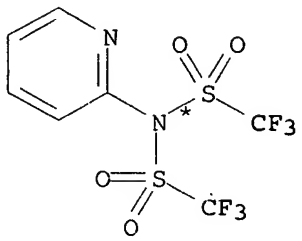
EY

RX(83) RCT EX 126162-38-7, EM 100-39-0, EN 600-00-0
RGT EP 7646-69-7 NaH
PRO EY 644985-53-5
CAT 311-28-4 Bu4N.I
SOL 109-99-9 THF

RX(84) OF 205 ...EO + EZ ===> FA...

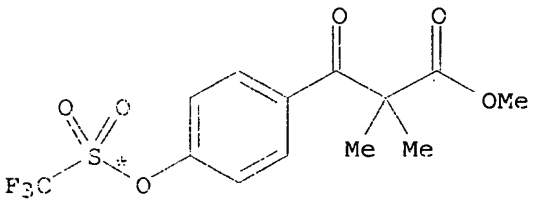



EO




EZ

(84)



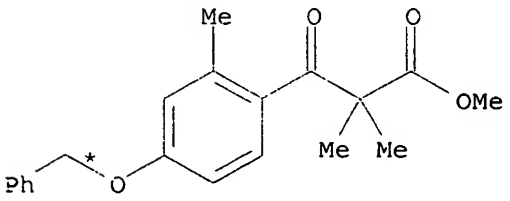

FA

RX(84) RCT EO 644985-49-9

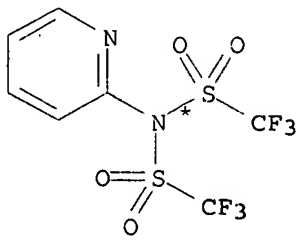
STAGE(1)
RGT G 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(2)
RCT EZ 145100-50-1
RGT FB 40949-94-8 K [N(SiMe3)2]
SOL 109-99-9 THF
PRO FA 644985-54-6

RX(85) OF 205 ...ES + EZ ===> A...

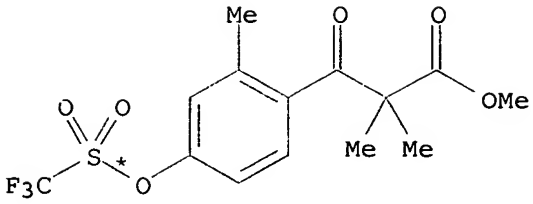



ES




EZ

(85)



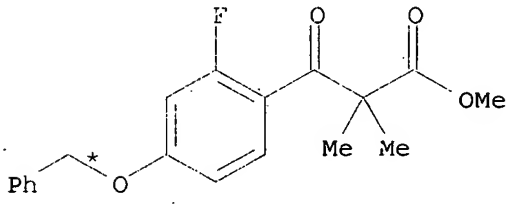
A

RX(85) RCT ES 644985-50-2

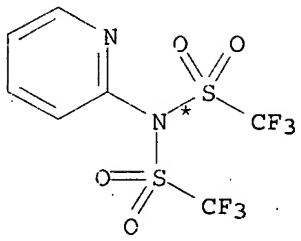
STAGE(1)
RGT G 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(2)
RCT EZ 145100-50-1
RGT FB 40949-94-8 K [N(SiMe3)2]
SOL 109-99-9 THF
PRO A 644985-55-7

RX(86) OF 205 ...EU + EZ ===> P...

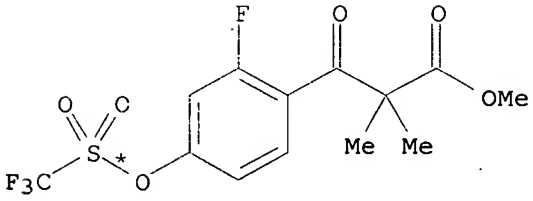


EU



EZ

(86)



P

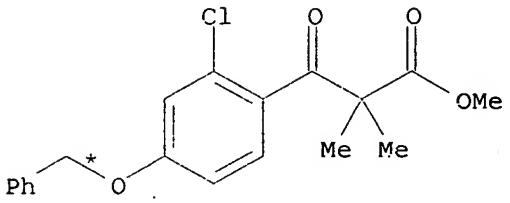
RX(86) RCT EU 644985-51-3

STAGE(1)
RGT G 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

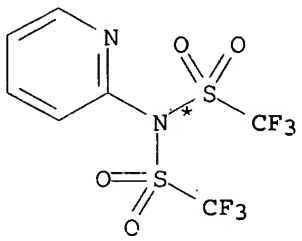
STAGE(2)

RCT EZ 145100-50-1
RGT FB 40949-94-8 K [N(SiMe3)2]
SOL 109-99-9 THF
PRO P 644985-56-8

RX(87) OF 205 ...EW + EZ ===> FC...

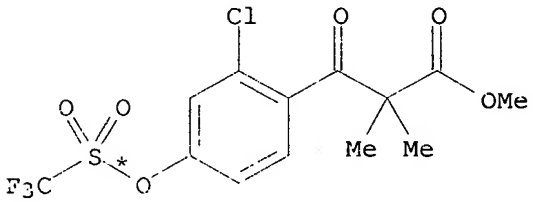


EW



EZ

(87) ⟶



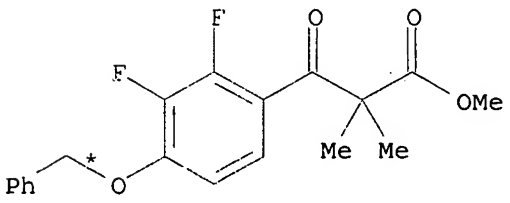
FC

RX(87) RCT EW 644985-52-4

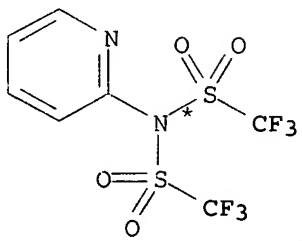
STAGE(1)
RGT G 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(2)
RCT EZ 145100-50-1
RGT FB 40949-94-8 K [N(SiMe3)2]
SOL 109-99-9 THF
PRO FC 644985-57-9

RX(88) OF 205 ...EY + EZ ===> FD...

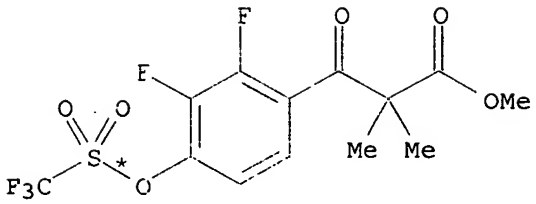


EY



EZ

(88) ⟶



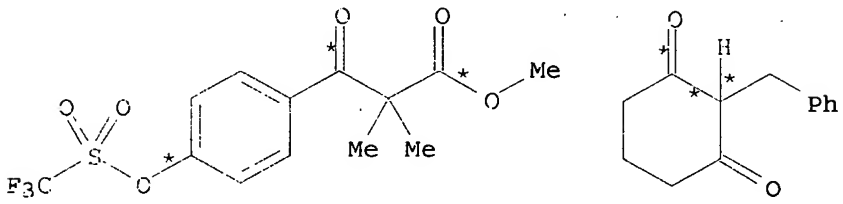
FD

RX(88) RCT EY 644985-53-5

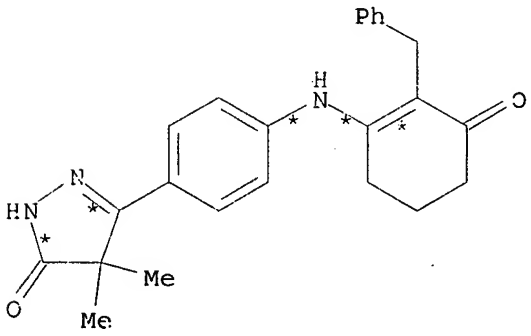
STAGE(1)
RGT G 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(2)
RCT EZ 145100-50-1
RGT FB 40949-94-8 K [N(SiMe3)2]
SOL 109-99-9 THF
PRO FD 644985-58-0

RX(89) OF 205 ...FA + AO ===> EF



FA AO (89)



EF

RX(89) RCT FA 644985-54-6

STAGE(1)

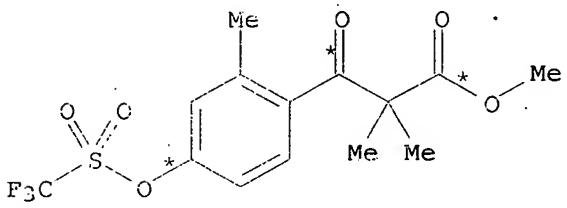
RGT D 621-84-1 Carbamic acid, phenylmethyl ester, E 534-17-8 Cs2CO3
CAT 51364-51-3 Ph2-pentadienone Pd, 161265-03-8 Phosphine, (9,9-dimethyl-9H-xanthene-4,5-diyl)bis[diphenyl-
SOL 109-99-9 THF

STAGE(2)
RGT F 302-01-2 N2H4
SOL 64-17-5 EtOH

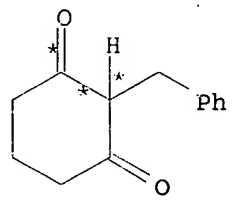
STAGE(3)
RGT G 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(4)
RCT AO 22381-56-2
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe, 67-68-5 DMSO
PRO EF 644985-35-3
NTE Buchwald reaction first stage, alternate prepn. also described

RX(90) OF 205 ...A + AO ===> EG

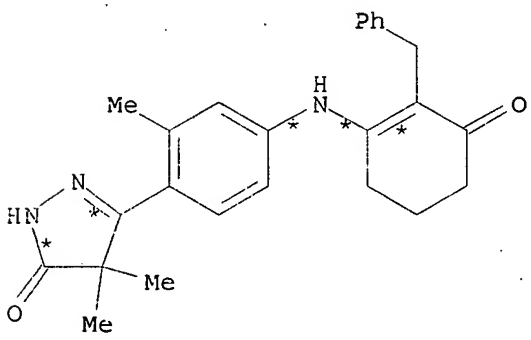



A




AO

(90)




EG

RX(90) RCT A 644985-55-7

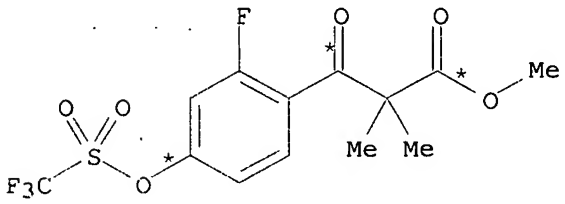
STAGE(1)
RGT D 621-84-1 Carbamic acid, phenylmethyl ester, E 534-17-8 Cs2CO3
CAT 51364-51-3 Ph2-pentadienone Pd, 161265-03-8 Phosphine, (9,9-dimethyl-9H-xanthene-4,5-diyl)bis[diphenyl-
SOL 109-99-9 THF

STAGE(2)
RGT F 302-01-2 N2H4
SOL 64-17-5 EtOH

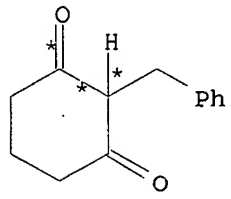
STAGE(3)
RGT G 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(4)
RCT AO 22381-56-2
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe, 67-68-5 DMSO
PRO EG 644985-36-4
NTE Buchwald reaction first stage, alternate prepn. also described

RX(91) OF 205 ...P + AO ===> EH

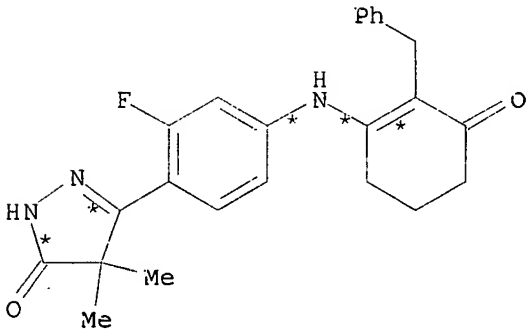


P



AO

(91)



EH

RX(91) RCT P 644985-56-8

STAGE(1)
RGT D 621-84-1 Carbamic acid, phenylmethyl ester, E 534-17-8 Cs2CO3
CAT 51364-51-3 Ph2-pentadienone Pd, 161265-03-8 Phosphine, (9,9-dimethyl-9H-xanthene-4,5-diyl)bis[diphenyl-
SOL 109-99-9 THF

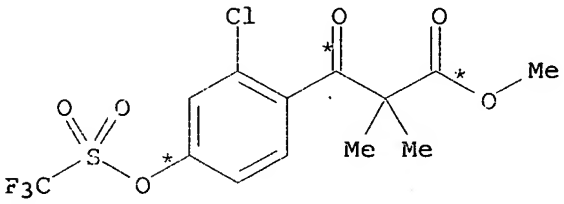
STAGE(2)
RGT F 302-01-2 N2H4
SOL 64-17-5 EtOH

STAGE(3)
RGT G 1333-74-0 H2

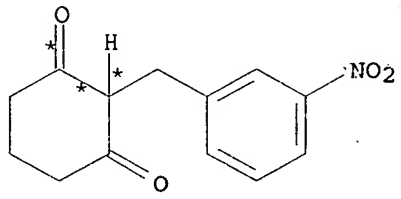
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(4)
RCT AO 22381-56-2
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe, 67-68-5 DMSO
PRO EH 644985-38-6
NTE Buchwald reaction first stage, alternate prepn. also described

RX(92) OF 205 ...FC + R ===> EI

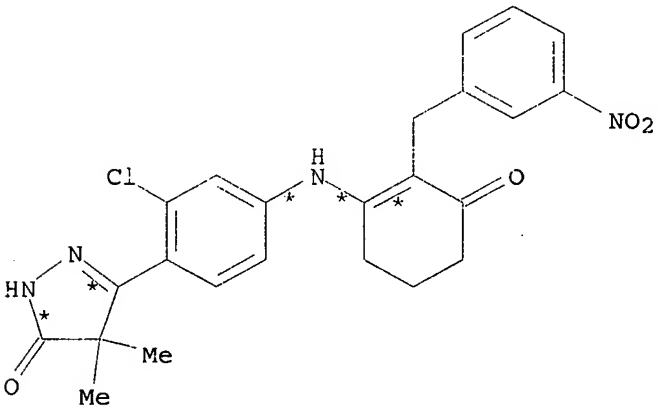


FC



R

(92)



EI

RX(92) RCT FC 644985-57-9

STAGE(1)
RGT D 621-84-1 Carbamic acid, phenylmethyl ester, E 534-17-8 Cs2CO3
CAT 51364-51-3 Ph2-pentadienone Pd, 161265-03-8 Phosphine, (9,9-dimethyl-9H-xanthene-4,5-diyl)bis[diphenyl-
SOL 109-99-9 THF

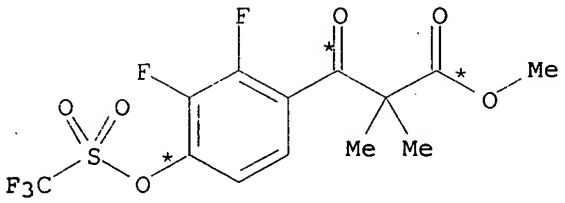
STAGE(2)
RGT F 302-01-2 N2H4
SOL 64-17-5 EtOH

STAGE(3)

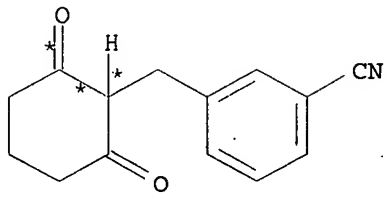
RGT G 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(4)
RGT R 724453-07-0
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe, 67-68-5 DMSO
PRO EI 644985-46-6
NTE Buchwald reaction first stage, alternate prepn. also described

RX(93) OF 205 ...FD + B ===> EK

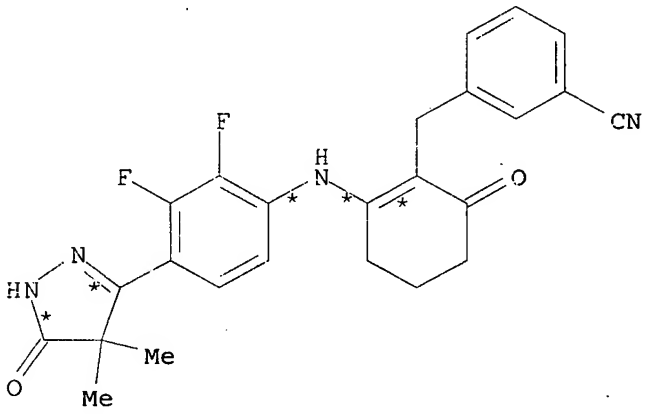


FD



B

(93)



EK

RX(93) RCT FD 644985-58-0

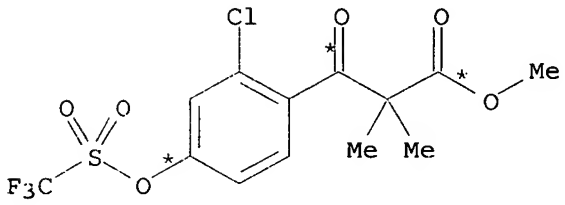
STAGE(1)
RGT D 621-84-1 Carbamic acid, phenylmethyl ester, E 534-17-8 Cs2CO3
CAT 51364-51-3 Ph2-pentadienone Pd, 161265-03-8 Phosphine, (9,9-dimethyl-9H-xanthene-4,5-diyl)bis[diphenyl-
SOL 109-99-9 THF

STAGE(2)
RGT F 302-01-2 N2H4
SOL 64-17-5 EtOH

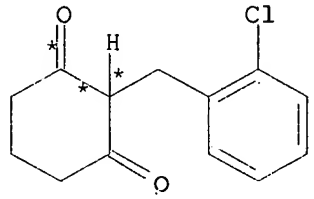
STAGE(3)
RGT G 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(4)
RCT B 724453-04-7
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe, 67-68-5 DMSO
PRO EK 644985-48-8
NTE Buchwald reaction first stage, alternate prepn. also described

RX(94) OF 205 ...FC + T ===> EJ

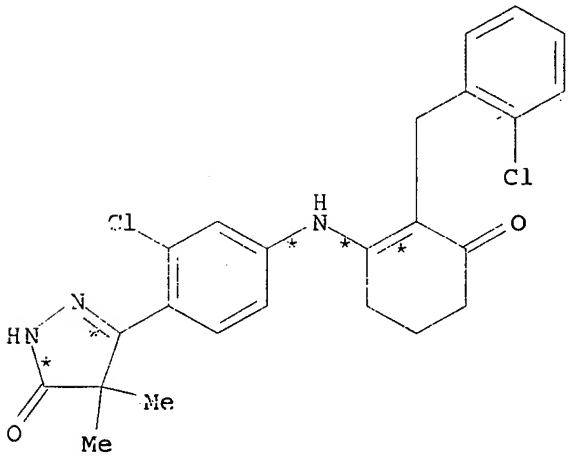


FC



T

(94)



EJ

RX(94) RCT FC 644985-57-9

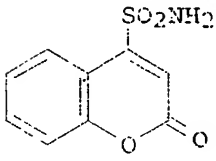
STAGE(1)
RGT D 621-84-1 Carbamic acid, phenylmethyl ester, E 534-17-8 Cs2CO3
CAT 51364-51-3 Ph2-pentadienone Pd, 161265-03-8 Phosphine, (9,9-dimethyl-9H-xanthene-4,5-diyl)bis[diphenyl-
SOL 109-99-9 THF

STAGE(2)
RGT F 302-01-2 N2H4
SOL 64-17-5 EtOH

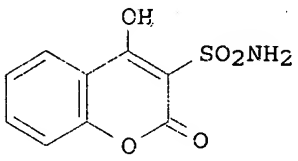
STAGE(3)
RGT G 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(4)
RCT T 724453-16-1
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe, 67-68-5 DMSO
PRO EJ 644985-47-7
NTE Buchwald reaction first stage, alternate prepn. also described

L2 ANSWER 43 OF 150 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 138:106511 CASREACT
TITLE: Synthesis of coumarin sulfonamides and sulfonylurea
AUTHOR(S): Kovac, Martin; Sabatie, Andrea; Floch, L'ubomir
CORPORATE SOURCE: Dep. Org. Chem., Fac. Chem. Technol., Slovak Univ. of Technol., Bratislava, SK-812 37, Slovakia
SOURCE: ARKIVOC (Gainesville, FL, United States) [online computer file] (2001), (6), 100-108
CODEN: AGFUAR
URL: http://www.arkat-usa.org/ark/journal/Volume2/Part3/Abramovitch/RA-216S/RA-216S.pdf
PUBLISHER: Arkat USA Inc.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
CLASSIFICATION: 26-4 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 5
GRAPHIC IMAGE:




I

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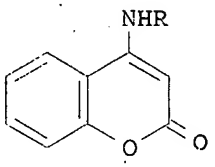



III

ABSTRACT:
4-Coumarinsulfonamide (I) and 4-hydroxy-3-coumarinsulfonamide (II), were prepared from 4-hydroxycoumarin. Coumarin-4-sulfonamide (I) was served as intermediate for the synthesis of N-(isopropylphenyl)-N-(coumarin-4-sulfonyl)urea 9 and N-(4-bromphenyl-), III (R = C6H4Br-4), N-(1,3,4-thiadiazol-2-yl-), III (R = 1,3,4-thiadiazol-2-yl), and N-(4-isopropylphenyl)-4-aminocoumarin III (R = C6H4CHMe2-4).

SUPPL. TERM: coumarin sulfonamide sulfonylurea prepn; hydroxycoumarin conversion sulfonamide sulfonylurea arylaminocoumarin heteroarylcoumarin
INDEX TERM: Flavonoids
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(coumarin sulfonamides and sulfonylurea; synthesis of coumarin sulfonamides and sulfonylurea as potential herbicides)
INDEX TERM: Sulfuration
(of 4-chlorocoumarin with mercaptans in the; synthesis of aminocoumarins, coumarin sulfonamides and sulfonylurea as potential herbicides)
INDEX TERM: Amination
(of 4-coumarinsulfonamide in the; synthesis of aminocoumarins, coumarin sulfonamides and sulfonylurea as potential herbicides)
INDEX TERM: Chlorination
Chlorosulfonylation

(of 4-hydroxycoumarin in the; synthesis of coumarin sulfonamides and sulfonylurea as potential herbicides)

INDEX TERM: Amidation
(of coumarinsulfonyl chlorides in the; synthesis of aminocoumarins, coumarin sulfonamides and sulfonylurea as potential herbicides)

INDEX TERM: 26907-41-5, Phenyl N-(1,3,4-thiadiazol-2-yl)carbamate
50882-29-6
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(amination by, of coumarin-4-sulfonamide; synthesis of coumarin sulfonamides and sulfonylurea as potential herbicides)

INDEX TERM: 1076-38-6, 4-Hydroxycoumarin
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(chlorination or chlorosulfonylation of; synthesis of coumarin sulfonamides and sulfonylurea as potential herbicides)

INDEX TERM: 5117-56-6P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(formation during attempted oxidation of 4-(ethylthio)coumarin with chlorine; synthesis of coumarin sulfonamides and sulfonylurea as potential herbicides)

INDEX TERM: 19345-55-2P, 4-Chloro-3,4':3',4''-tercoumarin
ROLE: BYP (Byproduct); PREP (Preparation)
(formation of during oxidation of hydroxycoumarin with chlorine in acetic acid; synthesis of coumarin sulfonamides and sulfonylurea as potential herbicides)

INDEX TERM: 18633-87-9P, 4-Hydroxy-3-coumarinsulfonyl chloride
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and amidation of, with ammonia; synthesis of coumarin sulfonamides and sulfonylurea as potential herbicides)

INDEX TERM: 485322-82-5P, 4-Coumarinsulfonyl chloride
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(preparation and amidation of, with tert-Bu amine; synthesis of coumarin sulfonamides and sulfonylurea as potential herbicides)

INDEX TERM: 485322-94-9P, 4-Coumarinsulfonamide
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and amination or acylation by, of coumarin-4-sulfonamide; synthesis of coumarin sulfonamides and sulfonylurea as potential herbicides)

INDEX TERM: 27066-05-3P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and attempted oxidation of, chlorination during; synthesis of coumarin sulfonamides and sulfonylurea as potential herbicides)

INDEX TERM: 18633-78-8P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and chlorination of; synthesis of coumarin sulfonamides and sulfonylurea as potential herbicides)

INDEX TERM: 485322-90-5P, N-(tert-Butyl)-4-coumarinsulfonamide
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and dealkylation of; synthesis of coumarin sulfonamides and sulfonylurea as potential herbicides)

INDEX TERM: 27129-30-2P, 4-(Isopropylthio)coumarin
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and oxidation of, with chlorine in acetic acid; synthesis of coumarin sulfonamides and sulfonylurea as potential herbicides)

INDEX TERM: 17831-88-8P, 4-Chlorocoumarin
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and sulfuration of, with thiols; synthesis of coumarin sulfonamides and sulfonylurea as potential herbicides)

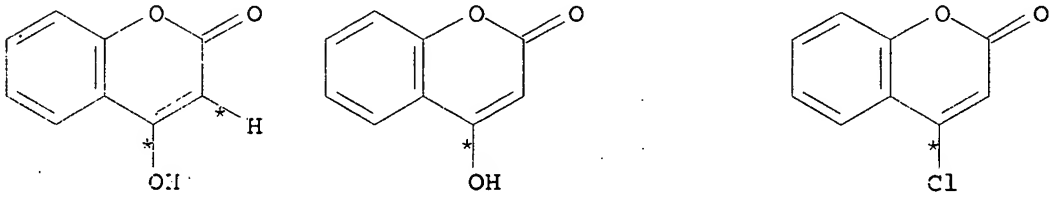
INDEX TERM: 31027-31-3, 4-Isopropylphenyl isocyanate
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reactions of, with coumarinsulfonamide; synthesis of coumarin sulfonamides and sulfonylurea as potential herbicides)

INDEX TERM: 18633-88-0P, 4-Hydroxy-3-coumarinsulfonamide 485322-87-0P, 4-[(4-Bromphenyl)amino]coumarin 485322-89-2P
485322-91-6P, 4-[(1,3,4-Thiadiazol-2-yl)amino]coumarin
485322-96-1P, 4-[(4-Isopropylphenyl)amino]coumarin
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of coumarin sulfonamides and sulfonylurea as potential herbicides)

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD.

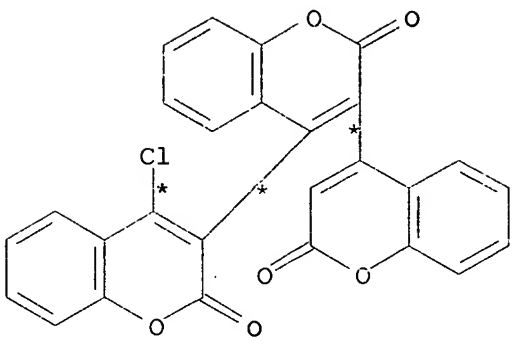

REFERENCE(S):
(1) Anon; Part of the Master Thesis of M K, Slovak University of Technology 1998
(2) Beyer, E; Sulfonylureas" in Herbicides. Chemistry, Degradation and Mode of Action 1988
(3) Checchi, S; Gazz Chim Ital 1967, V97, P1749 CAPLUS
(4) Hay, J; Pestic Sci 1990, V29, P247 CAPLUS
(5) Knight, A; Can J Chem 1968, V46, P2495 CAPLUS
(6) Levitt, G; ACS Symposium Series 1991, V443, P16 CAPLUS
(7) Meyer, W; US 4419121 1983 CAPLUS
(8) Newman, M; J Am Chem Soc 1959, V81, P2266 CAPLUS
(9) Peinhardt, G; Pharmazie 1970, V25, P68 CAPLUS
(10) Spalding, D; J Am Chem Soc 1950, V72, P5338 CAPLUS
(11) Zacharov, P; Zhurnal Org Khimii 1971, V7(2), P388


RX(1) OF 55 4 A ===> B + C...




2 A + 2 A —(1)→ B

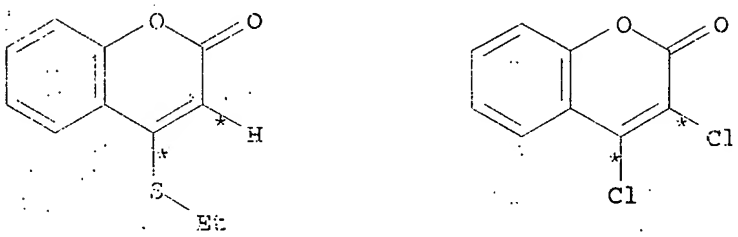
YIELD 55%



C
YIELD 17%

RX(1) RCT A 1076-38-6
RGT D 10025-87-3 POCl3
PRO B 17831-88-8, C 19345-55-2
SOL 10025-87-3 POCl3

RX(2) OF 55 ...E ===> F



E (2) F
YIELD 55%

RX(2) RCT E 27066-05-3

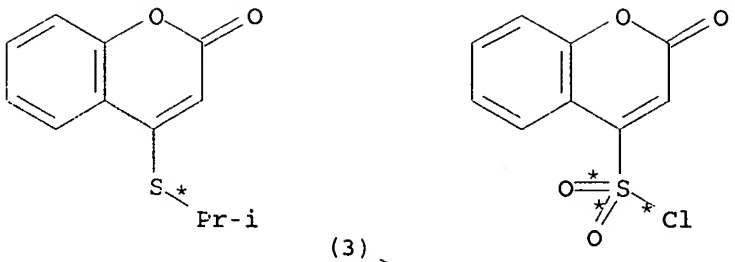
STAGE(1)
RGT G 7732-18-5 Water
SOL 64-19-7 AcOH

STAGE(2)
RGT H 7782-50-5 Cl2

STAGE(3)
RGT G 7732-18-5 Water

STAGE(4)
RGT H 7782-50-5 Cl2
PRO F 5117-56-6

RX(3) OF 55 ...J ===> K...



J

(3)

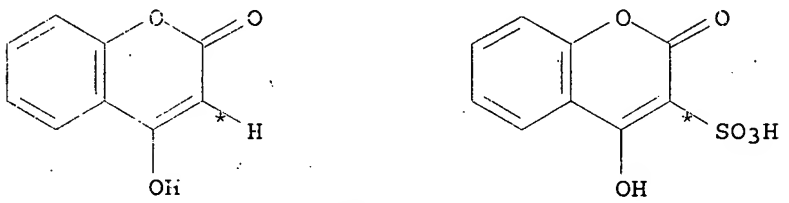
K
YIELD 84%

RX(3) RCT J 27129-30-2

STAGE(1)
RGT G 7732-18-5 Water
SOL 64-19-7 AcOH

STAGE(2)
RGT L 7778-50-9 K2Cr2O7, M 7647-01-0 HCl, G 7732-18-5 Water
PRO K 485322-82-5

RX(4) OF 55 A ===> N...



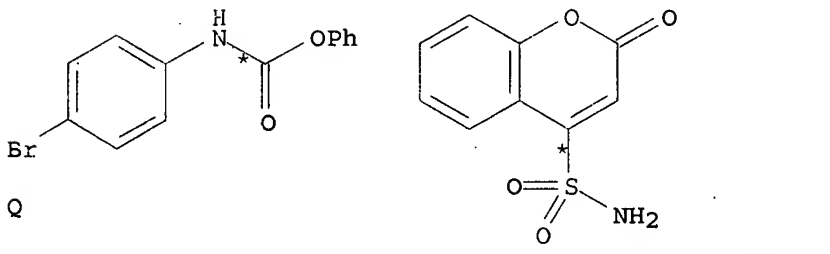
A

(4)

N
YIELD 91%

RX(4) RCT A 1076-38-6
RGT O 7790-94-5 ClSO3H
PRO N 18633-78-8
SOL 123-91-1 Dioxane

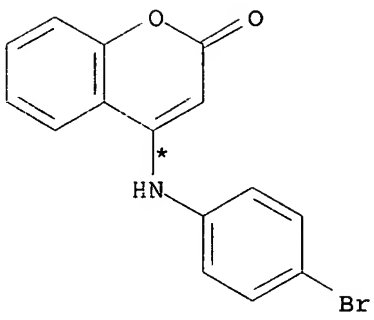
RX(5) OF 55 ...Q + R ===> S



Q

R

(5)



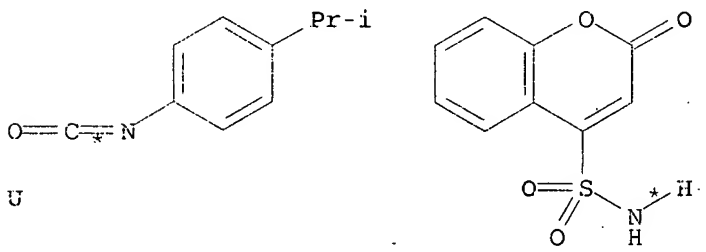
S
YIELD 42%

RX(5) RCT Q 50882-29-5, R 485322-94-9

STAGE(1)
RGT T 6674-22-2 DBU

STAGE(2)
RGT M 7647-01-0 HCl
SOL 7732-18-5 Water
PRO S 485322-87-0

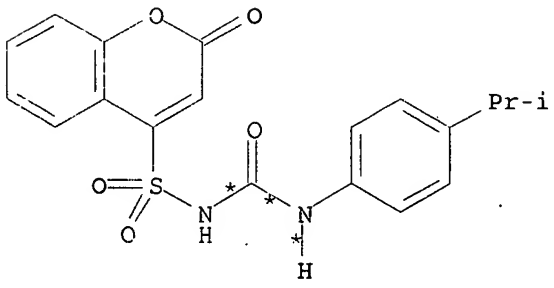
RX(6) OF 55 ...U + R ===> V



U

R

(6)



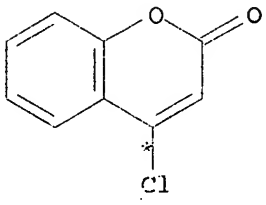
V
YIELD 46%

RX(6) RCT U 31027-31-3, R 485322-94-9

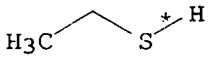
STAGE(1)
RGT W 7646-78-8 SnCl4

STAGE(2)
RGT M 7647-01-0 HCl
SOL 7732-18-5 Water, 141-78-6 AcOEt
PRO V 485322-89-2

RX(7) OF 55 ...B + Y ===> E...

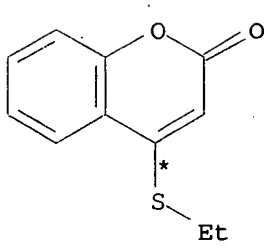


B



Y

(7)



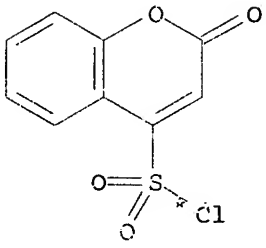
E
YIELD 85%

RX(7) RCT E 17831-38-8

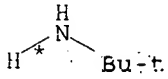
STAGE(1)
SOL 67-56-1 MeOH

STAGE(2)
RCT Y 75-08-1
RGT Z 7440-23-5 Na
SOL 67-56-1 MeOH
PRO B 27066-05-3

RX(8) OF 55 ...K + AB ===> AC...

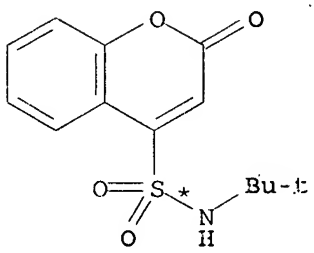


K



AB

(8)



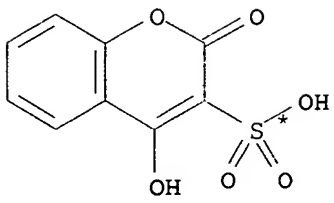
AC
YIELD 34%

RX(8) RCT K 485322-82-5

STAGE(1)
SOL 67-66-3 CHCl3

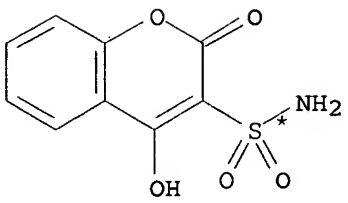
STAGE(2)
RCT AB 75-64-9
SOL 67-66-3 CHCl3
PRO AC 485322-90-5

RX(9) OF 55 ...N ===> AE



N

(9)



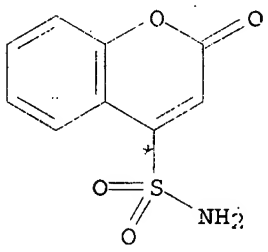
AE
YIELD 10%

RX(9) RCT N 18633-78-8

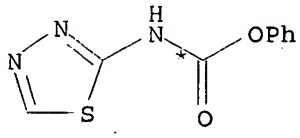
STAGE(1)
RGT AF 7719-09-7 SOCl2
SOL 7719-09-7 SOCl2

STAGE(2)
RGT AG 7664-41-7 NH3
SOL 67-56-1 MeOH
PRO AE 18633-88-0

RX(10) OF 55 ...R + AH ===> AI

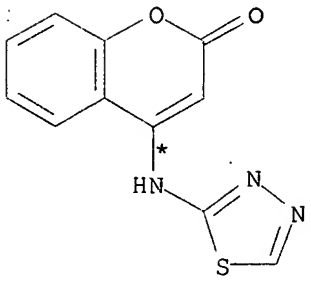


R



AH

(10)



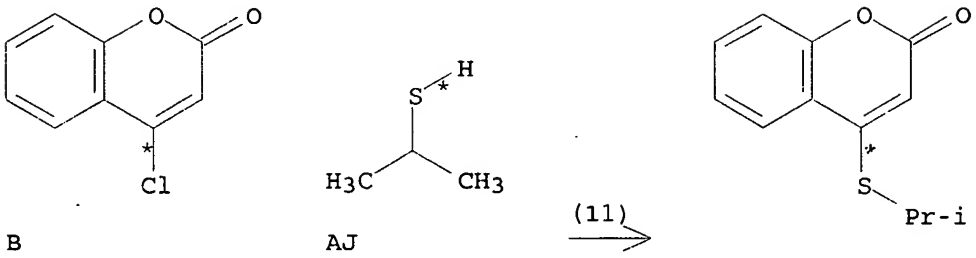
AI
YIELD 82%

RX(10) RCT R 485322-94-9, AH 26907-41-5

STAGE(1)
RGT T 6674-22-2 DBU

STAGE(2)
RGT M 7647-01-0 HCl
SOL 7732-18-5 Water
PRO AI 485322-91-6

RX(11) OF 55 ...B + AJ ===> J...



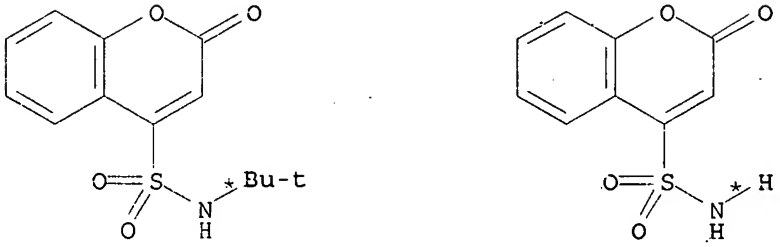

B AJ J
YIELD 64%

RX(11) RCT B 17831-88-8, AJ 75-33-2

STAGE(1)
SOL 67-56-1 MeOH

STAGE(2)
RGT Z 7440-23-5 Na
SOL 67-56-1 MeOH
PRO J 27129-30-2

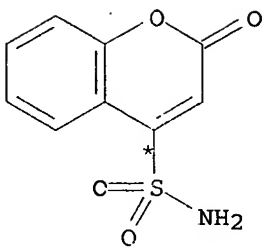
RX(12) OF 55 ...AC ===> R...



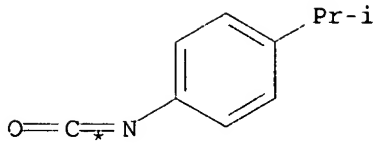

AC R
YIELD 40%

RX(12) RCT AC 485322-90-5
RGT AK 76-05-1 F3CCO2H
PRO R 485322-94-9
SOL 76-05-1 F3CCO2H

RX(13) OF 55 ...R + U ===> AL

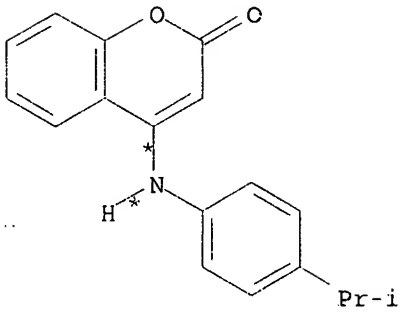


R



U

(13)



AL
YIELD 65%

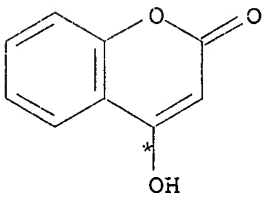
RX(13) RCT R 485322-94-9

STAGE(1)
SOL 123-91-1 Dioxane

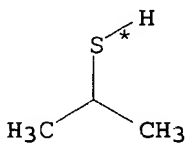
STAGE(2)
RCT U 31027-31-3
RGT AM 3001-72-7 DBN (heterocycle)

STAGE(3)
RGT M 7647-01-0 HCl
SOL 7732-18-5 Water
PRO AL 485322-96-1

RX(14) OF 55 A + AJ ===> J...

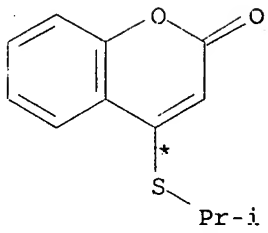


A



AJ

(14)



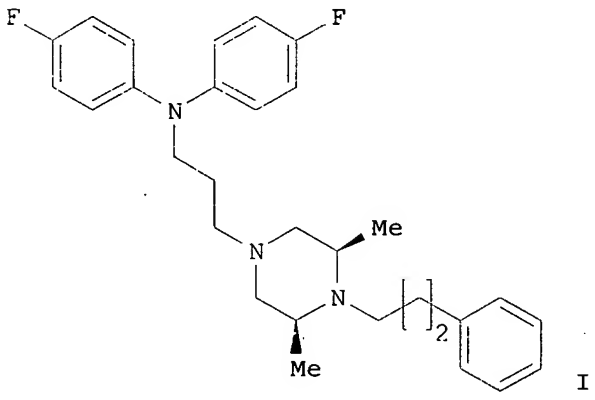
J
YIELD 28%

RX(14) RCT A 1076-38-6

STAGE(1)
RGT AN 121-44-8 Et3N
CAT 1122-58-3 4-DMAP
SOL 67-64-1 Me2CO

STAGE(2)
RCT AJ 75-33-2
PRO J 27129-30-2

L2 ANSWER 67 OF 150 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 136:318809 CASREACT
TITLE: [3-cis-3,5-Dimethyl-(1-piperazinyl)alkyl]-bis-(4'-fluorophenyl)amine analogues as novel probes for the dopamine transporter
AUTHOR(S): Cao, Jianjing; Husbands, Stephen M.; Kopajtic, Theresa; Katz, Jonathan L.; Newman, Amy Hauck
CORPORATE SOURCE: Medicinal Chemistry Section, National Institute on Drug Abuse - Intramural Research Program, Baltimore, MD, 21224, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(24), 3169-3173
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 1-3 (Pharmacology)
Section cross-reference(s): 2, 28
GRAPHIC IMAGE:



I

ABSTRACT:
In a continuing effort to identify novel probes with which to study the dopamine transporter (DAT), the authors discovered that the σ receptor antagonist, rimcazole, binds with moderate affinity (Ki=224 nM) to the DAT. The results from previous SAR studies suggested that substitution of the carbazole ring system of rimcazole with bis-(4'-fluorophenyl)amine might improve binding affinity and selectivity for the DAT. Thus, a novel series of [3-cis-3,5-dimethyl-(1-piperazinyl)alkyl]bis-(4'-fluorophenyl)amines were synthesized. The most potent compound in this series I displaced [3H]WIN 35,428 binding in rat caudate-putamen (Ki=17.6 nM) with comparable affinity to GBR 12909. Despite high-affinity binding at DAT, and structural similarity to GBR 12909, preliminary studies suggest I behaves more like rimcazole than GBR 12909 and does not demonstrate cocaine-like psychostimulant behavior in mice.

SUPPL. TERM: dimethylpiperazinyl alkyl fluorophenylamine analog dopamine transporter probe

INDEX TERM: Structure-activity relationship
(dopamine transporter-binding; [cis-di-Me-(piperazinyl)alkyl](fluorophenyl)amine analogs as novel probes for dopamine transporter in relation to behavior effects)

INDEX TERM: Transport proteins
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(dopamine transporter; [cis-di-Me-(piperazinyl)alkyl](fluorophenyl)amine analogs as novel probes for dopamine transporter in relation to behavior effects)

INDEX TERM: Behavior
(locomotor; [cis-di-Me-(piperazinyl)alkyl](fluorophenyl)amine analogs as novel probes for dopamine transporter in relation to behavior effects)

INDEX TERM: 67469-78-7, GBR 12909 75859-04-0, Rimcazole
ROLE: PAC (Pharmacological activity); BIOL (Biological study)
([cis-di-Me-(piperazinyl)alkyl](fluorophenyl)amine analogs as novel probes for dopamine transporter in relation to behavior effects)

INDEX TERM: 251907-49-0, SH 2-21
ROLE: PAC (Pharmacological activity); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
([cis-di-Me-(piperazinyl)alkyl](fluorophenyl)amine analogs as novel probes for dopamine transporter in relation to behavior effects)

INDEX TERM: 409313-68-4P
ROLE: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
([cis-di-Me-(piperazinyl)alkyl](fluorophenyl)amine analogs as novel probes for dopamine transporter in relation to behavior effects)

INDEX TERM: 409313-72-0P 409313-73-1P
ROLE: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation).
([cis-di-Me-(piperazinyl)alkyl](fluorophenyl)amine analogs as novel probes for dopamine transporter in relation to behavior effects)

INDEX TERM: 460-00-4 645-45-4, Benzenepropanoyl chloride 6284-84-0, cis-2,5-Dimethylpiperazine 6831-55-6 15486-96-1, 3-Bromopropanoyl chloride 16744-99-3
ROLE: RCT (Reactant); RACT (Reactant or reagent)
([cis-di-Me-(piperazinyl)alkyl](fluorophenyl)amine analogs as novel probes for dopamine transporter in relation to behavior effects)

INDEX TERM: 330-91-6P 95017-63-3P 409313-67-3P 409313-69-5P 409313-70-8P 409313-71-9P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
([cis-di-Me-(piperazinyl)alkyl](fluorophenyl)amine analogs as novel probes for dopamine transporter in relation to behavior effects)

INDEX TERM: 808754-61-2
(preparation of)

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S):
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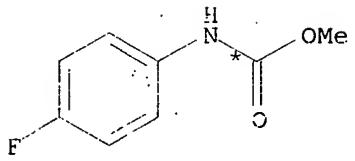
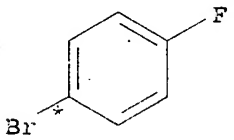
(29) Wise, L; J Med Chem 1985, V28, P606 CAPLUS
(30) Wise, R; Annu Rev Neurosci 1996, V19, P319 CAPLUS

RX(1) OF 35 **A** + **B** ===> **C**...

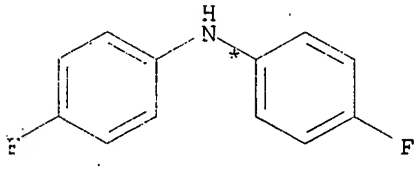



A




B

(1) →




C
YIELD 66%

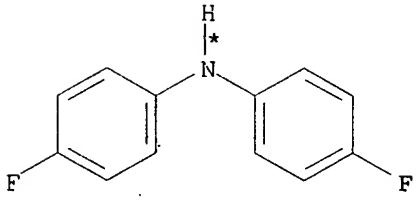
RX(1) RCT A **16744-99-3**, B **460-00-4**

STAGE(1)
RGT D 584-08-7 K2CO3
CAT 7681-65-4 CuI

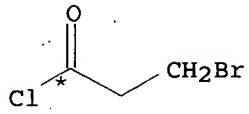
STAGE(2)
RGT E 1310-58-3 KOH
SOL 64-17-5 EtOH

PRO C 330-91-6
NTE reflux

RX(2) OF 35 ...C + H ===> I...

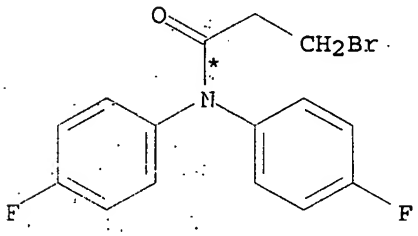


C



H

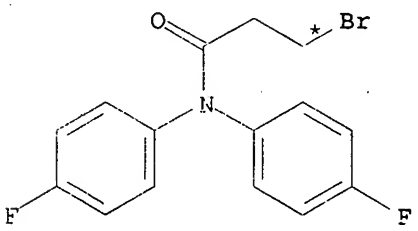
(2) →



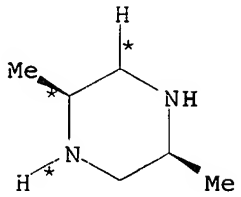
I
YIELD 83%

RX(2) RCT C 330-91-6, H 15486-96-1
PRO I 95017-63-3
SOL 71-43-2 Benzene
NTE reflux

RX(3) OF 35 ...I + K ===> L...

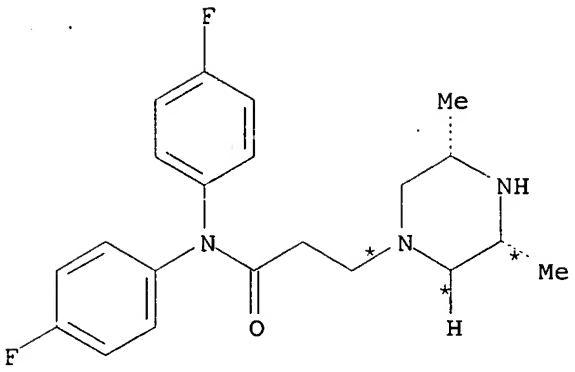


I



K

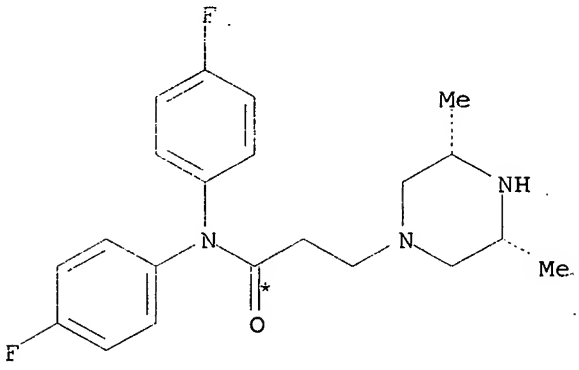
(3) →



L
YIELD 100%

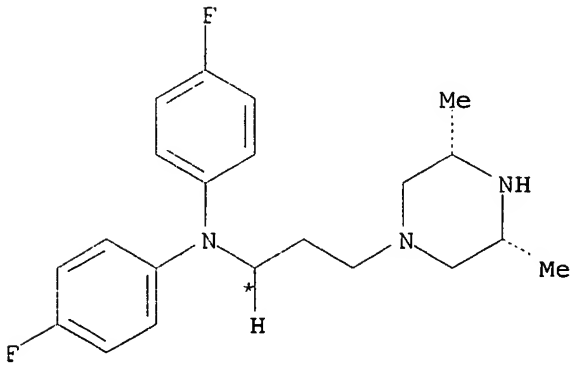
RX(3) RCT I 95017-63-3, K 6284-84-0
RGT D 584-08-7 K2CO3
PRO L 409313-67-3
SOL 68-12-2 DMF, 7732-18-5 Water

RX(4) OF 35 ...L ===> O...



L

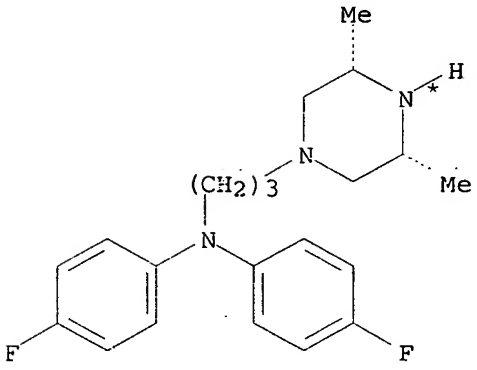
(4)



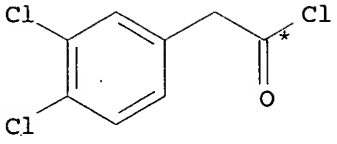
O
YIELD 77%

RX(4) RCT L 409313-67-3
RGT P 16853-85-3 LiAlH4
PRO O 409313-68-4
SOL 109-99-9 THF
NTE reflux

RX(5) OF 35 ...O + R ===> S...

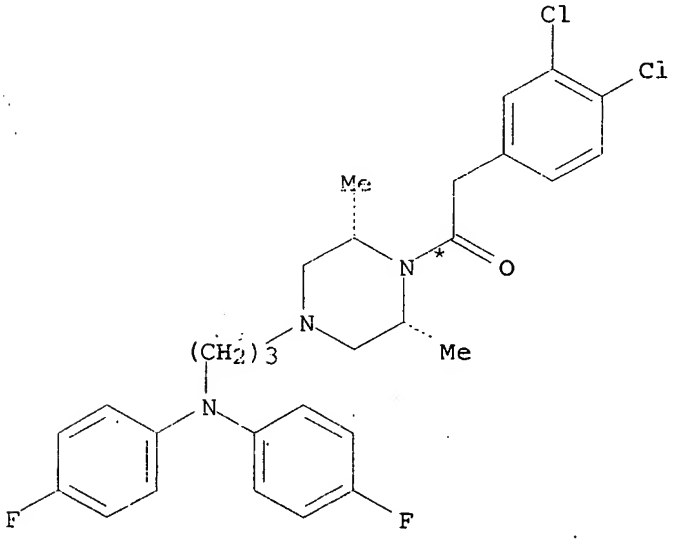



O




R

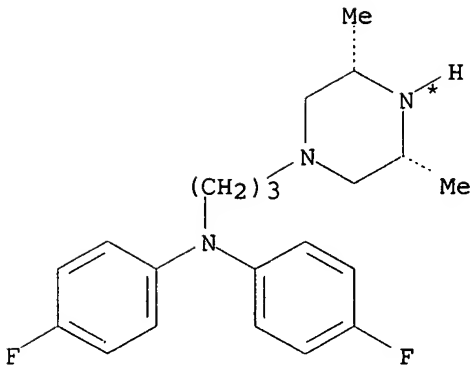
(5) ⟶



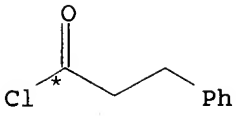

S

RX(5) RCT O 409313-68-4, R 6831-55-6
PRO S 409313-69-5
SOL 108-88-3 PhMe
NTE reflux

RX(6) OF 35 ...O + U ===> V...

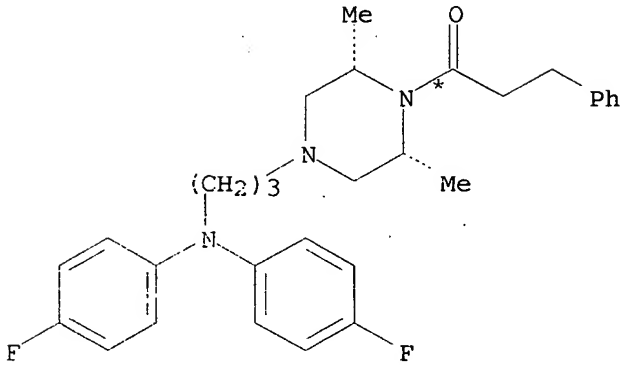


O



U

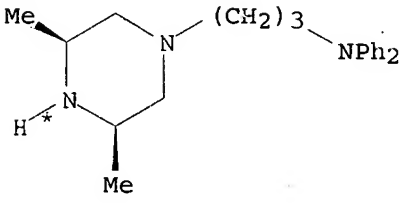
(6) →



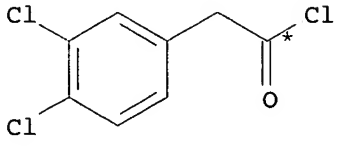
V

RX(6) RCT O 409313-68-4, U 645-45-4
PRO V 409313-70-8
SOL 108-88-3 PhMe
NTE reflux

RX(7) OF 35 W + R ===> X...

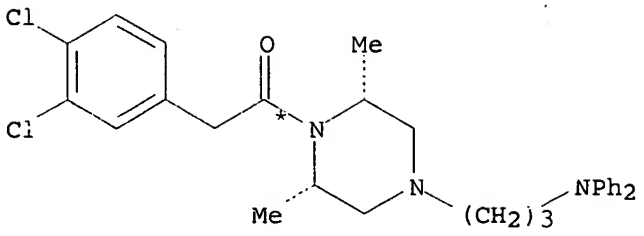


W



R

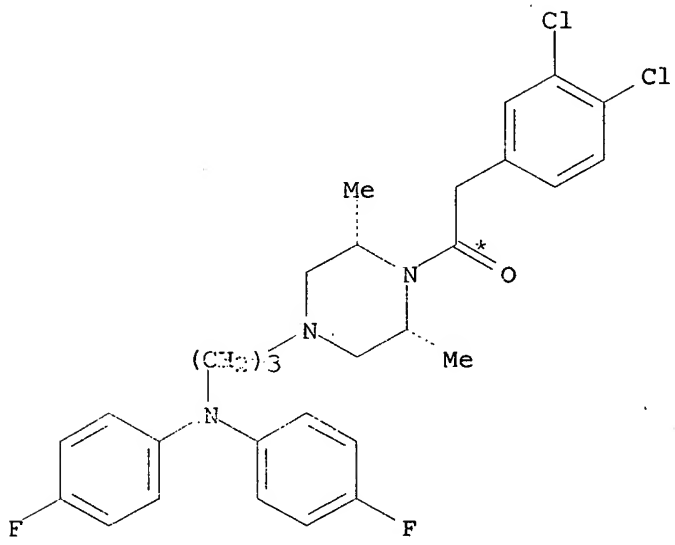
(7) →



X

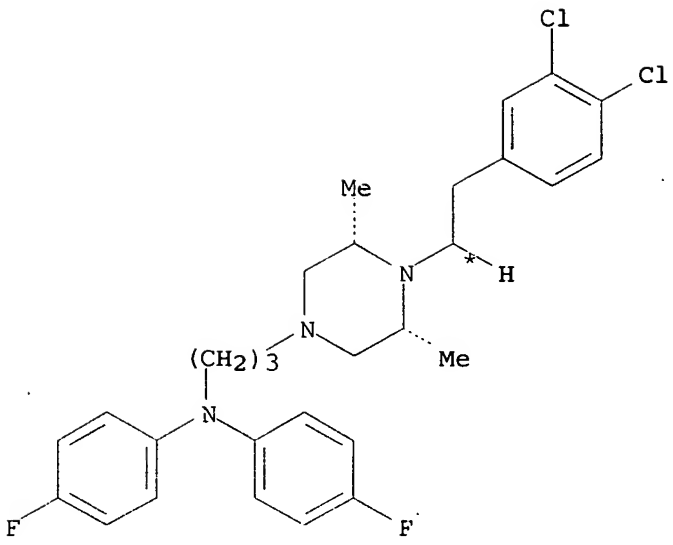
RX(7) RCT W 251907-49-0, R 6831-55-6
PRO X 409313-71-9
SOL 108-88-3 PhMe
NTE reflux

RX(8) OF 35 ...S ===> Y



S

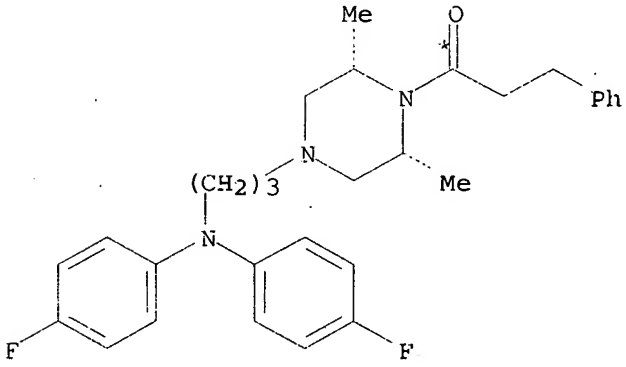
(8) →



Y

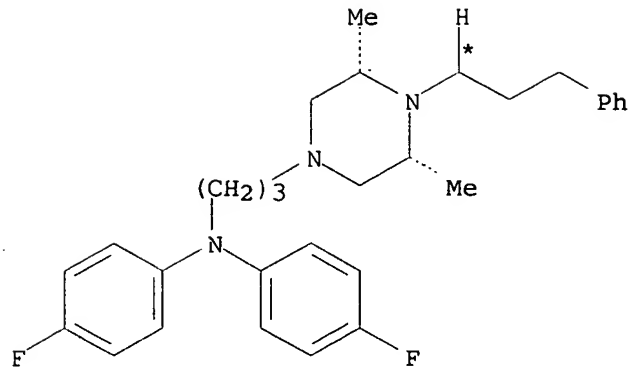
RX(8) RCT S 409313-69-5
RGT P 16853-85-3 LiAlH4
PRO Y 409313-72-0
SOL 109-99-9 THF
NTE reflux

RX(9) OF 35 ...V ===> Z



V

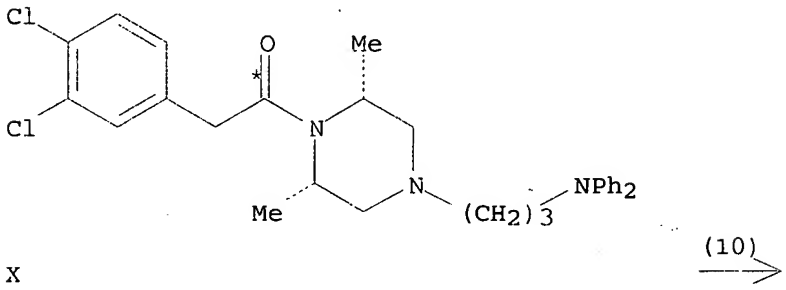
(9) ⟶



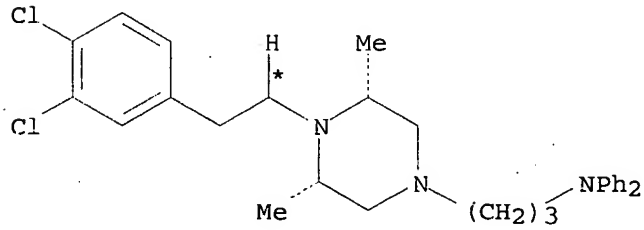
Z

RX(9) RCT V 409313-70-8
RGT P 16853-85-3 LiAlH4
PRO Z 409313-73-1
SOL 109-99-9 THF
NTE reflux

RX(10) OF 35 ...X ===> AA



X



AA

RX(10) RCT X 409313-71-9
RGT P 16853-85-3 LiAlH4
PRO AA 808754-61-2
SOL 109-99-9 THF
NTE reflux

L2 ANSWER 115 OF 150 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 124:290154 CASREACT

TITLE: Synthesis of nucleoside and related compounds. Part 38. Deamination of 9-(hydroxymethylated cycloalkyl)-9H-adenines (carbocyclic adenine nucleosides) by adenosine deaminase: effect of high-pressure upon deamination rate and enantioselectivity

AUTHOR(S): Katagiri, Nobuya; Ito, Yumiko; Shiraishi, Takuya; Maruyama, Tokumi; Sato, Yoshiko; Kaneko, Chikara

CORPORATE SOURCE: Pharmaceutical Inst., Tohoku Univ., Sendai, 980-77, Japan

SOURCE: Nucleosides & Nucleotides (1996), 15(1-3), 631-47
CODEN: NUNUD5; ISSN: 0732-8311

PUBLISHER: Dekker

DOCUMENT TYPE: Journal

LANGUAGE: English

CLASSIFICATION: 33-9 (Carbohydrates)
Section cross-reference(s): 7, 9

ABSTRACT:
The deamination of eight kinds of racemic carbocyclic adenine nucleosides by adenosine deaminase under high-pressure (400 MPa) was examined and the result was compared with that obtained from the reaction under atmospheric pressure. The deamination of all carbocyclic nucleosides irresp. to their ring size of carbocycles was facilitated remarkably by high-pressure. The reaction of three and five membered carboxylic nucleosides resulted in the very high enantioselectivity both under high- and atmospheric pressure whereas the enantioselectivity of six membered carbocyclic nucleosides was suppressed under high-pressure. However, the enantioselectivity of four membered nucleosides was low under both conditions.

SUPPL. TERM: pressure deaminase deamination carbocyclic nucleoside; enantioselective deaminase deamination carbocyclic nucleoside; carbocyclic nucleoside prepn deamination adenosine deaminase

INDEX TERM: Stereochemistry
(enantioselective deamination of carbocyclic adenine nucleosides by adenosine deaminase under high-pressure)

INDEX TERM: Nucleosides, preparation
ROLE: BPN (Biosynthetic preparation); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(enantioselective deamination of carbocyclic adenine nucleosides by adenosine deaminase under high-pressure)

INDEX TERM: Deamination
(enantioselective, under high-pressure; enantioselective deamination of carbocyclic adenine nucleosides by adenosine deaminase under high-pressure)

INDEX TERM: 174466-18-3P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(52% e.e. (absolute configuration undetd.); enantioselective deamination of carbocyclic adenine nucleosides by adenosine deaminase under high-pressure)

INDEX TERM: 174466-14-9P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(77% e.e. (absolute configuration undetd.); enantioselective deamination of carbocyclic adenine nucleosides by adenosine deaminase under high-pressure)

INDEX TERM: 175651-18-0P 175651-19-1P 175651-20-4P 175651-21-5P
175651-22-6P 175776-33-7P 175776-34-8P 175776-35-9P
ROLE: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(enantioselective deamination of carbocyclic adenine nucleosides by adenosine deaminase under high-pressure)

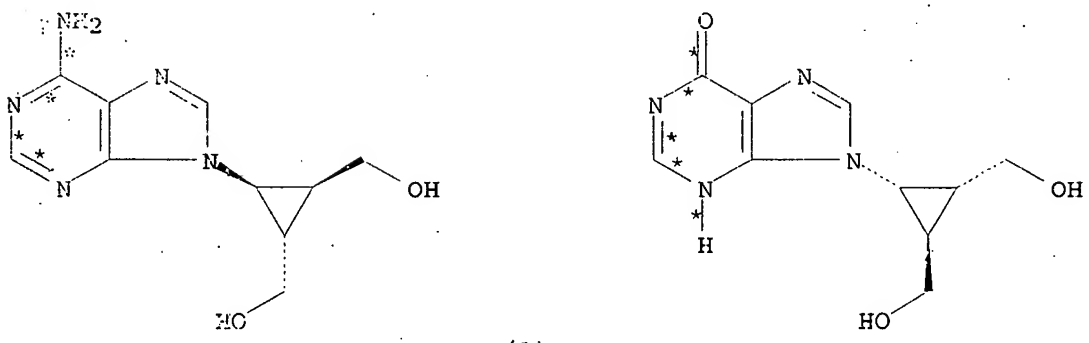
INDEX TERM: 9026-93-1, Adenosine deaminase
ROLE: CAT (Catalyst use); USES (Uses)
(enantioselective deamination of carbocyclic adenine nucleosides by adenosine deaminase under high-pressure)

INDEX TERM: 56-05-3, 2-Amino-4,6-dichloropyrimidine 592-57-4, 1,3-Cyclohexadiene 2028-74-2, 4-Chlorophenyldiazonium chloride 5413-85-4, 5-Amino-4,6-dichloropyrimidine 10310-21-1, 2-Amino-6-chloropurine 17257-71-5 20445-31-2 24224-99-5, Benzenesulfonyl cyanide 49805-30-3, 2-Azabicyclo[2.2.1]hept-5-en-3-one 124770-85-0 126261-74-3 132398-80-2 132487-14-0 140440-40-0
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(enantioselective deamination of carbocyclic adenine nucleosides by adenosine deaminase under high-pressure)

INDEX TERM: 39170-54-2P, 2-Azabicyclo[2.2.2]oct-5-en-3-one 118237-82-4P 118237-88-0P 122624-72-0P 124752-25-6P 126092-90-8P 129261-95-6P 153064-91-6P 162427-15-8P 174466-13-8P 174466-15-0P 174466-16-1P 175651-10-2P 175651-11-3P 175651-12-4P 175651-13-5P 175651-14-6P 175651-15-7P 175651-16-8P 175776-29-1P 175776-31-5P 175776-32-6P 202530-27-6P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(enantioselective deamination of carbocyclic adenine nucleosides by adenosine deaminase under high-pressure)

INDEX TERM: 151896-53-6P 175651-17-9P 175776-30-4P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(enantioselective deamination of carbocyclic adenine nucleosides by adenosine deaminase under high-pressure)

RX(1) OF 99 A ===> B

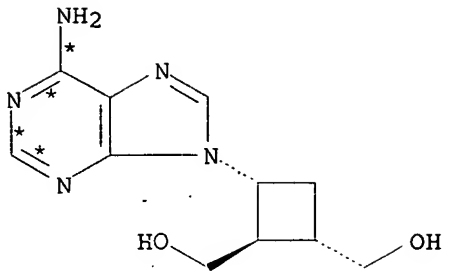



A

B
YIELD 50%

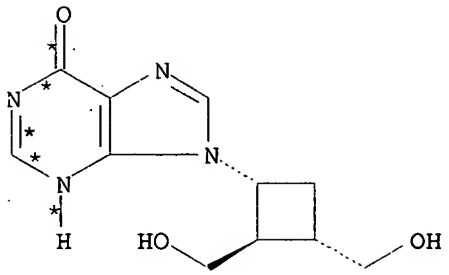
RX(1) RCT A 132398-80-2
PRO B 175651-17-9
CAT 9026-93-1 Adenosine deaminase
SOL 7732-18-5 Water
NTE buffered soln. Phosphate pH 7.0, biotransformation, enzymic, Adenosine deaminase type IV from calf intestinal mucosa used, alternative reaction conditions gave lower yield, stereoselective

RX(2) OF 99 E ===> F



E

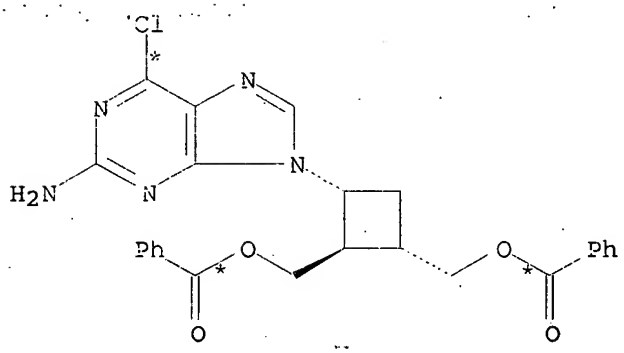
(2)



F
YIELD 35%

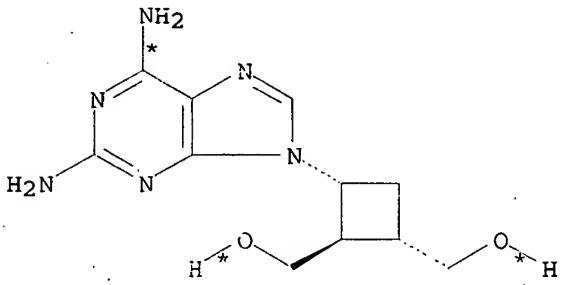
RX(2) RCT E 124770-85-0
PRO F 126092-90-8
CAT 9026-93-1 Adenosine deaminase
SOL 7732-18-5 Water
NTE buffered soln. Phosphate pH 7.0, biotransformation, enzymic, Adenosine deaminase type IV from calf intestinal mucosa used, alternative reaction conditions gave lower yield, high pressure, stereoselective

RX(3) OF 99 ...G ===> H...



G

(3)

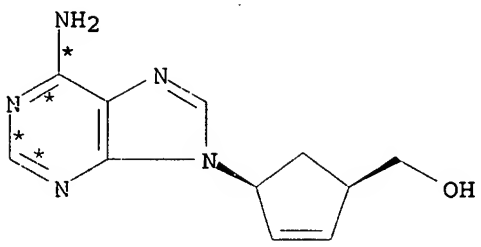


H
YIELD 77%

RX(3) RCT G 175776-29-1
RGT I 7664-41-7 NH3

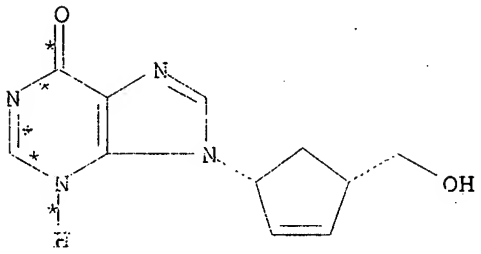
PRO H 129261-95-6
SOL 67-56-1 MeOH
NTE sealed tube used, stereoselective

RX(4) OF 99 K ===> L



K

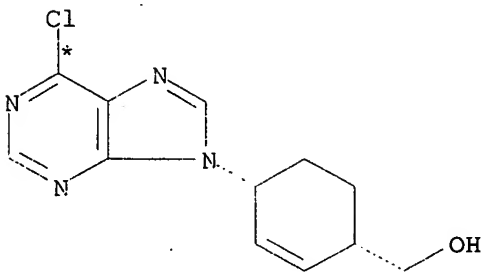
(4) ⟶



L
YIELD 48%

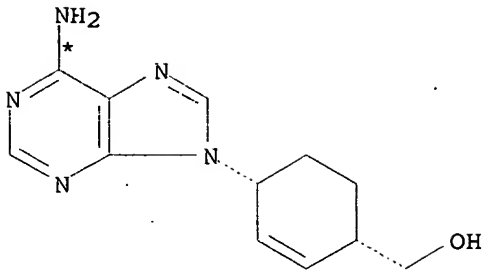
RX(4) RCT K 118237-82-4
PRO L 175776-31-5
CAT 9026-93-1 Adenosine deaminase
SOL 7732-18-5 Water
NTE buffered soln. Phosphate pH 7.0, biotransformation, enzymic, Adenosine deaminase type IV from calf intestinal mucosa used, alternative reaction conditions gave lower yield, high pressure, stereoselective

RX(5) OF 99 ...M ===> N...



M

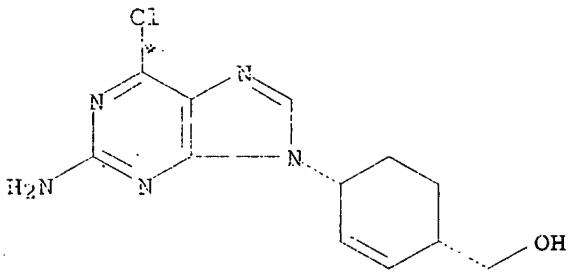
(5) ⟶



N
YIELD 74%

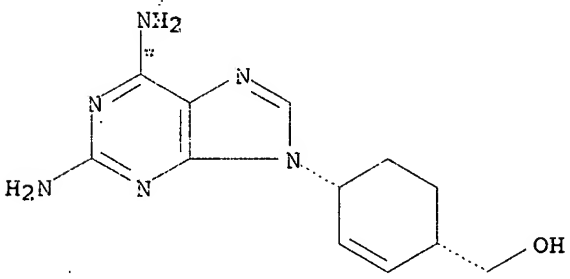
RX(5) RCT M 174466-13-8
RGT I 7664-41-7 NH3
PRO N 174466-15-0
SOL 67-56-1 MeOH
NTE sealed tube used

RX(6) OF 99 ...O ===> P...



O

(6)

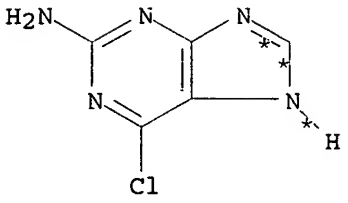


P
YIELD 52%

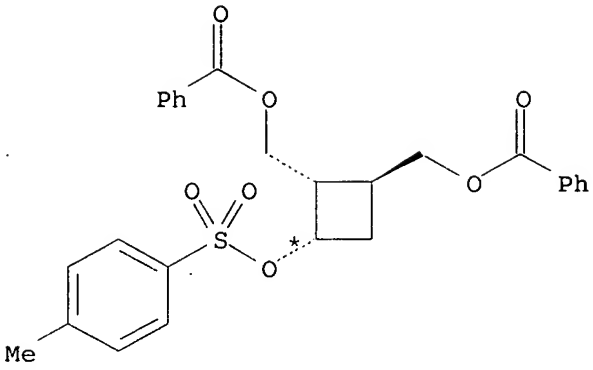
RX(6) RCT O 174466-16-1
RGT I 7664-41-7 NH3
PRO P 174466-18-3
SOL 67-56-1 MeOH

NTE sealed tube used

RX(7) OF 99 Q + R ===> G...

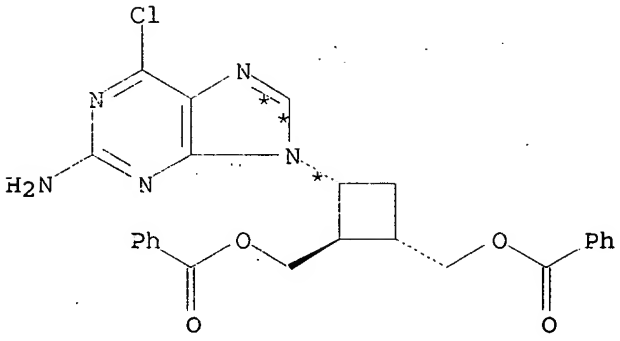


Q



R

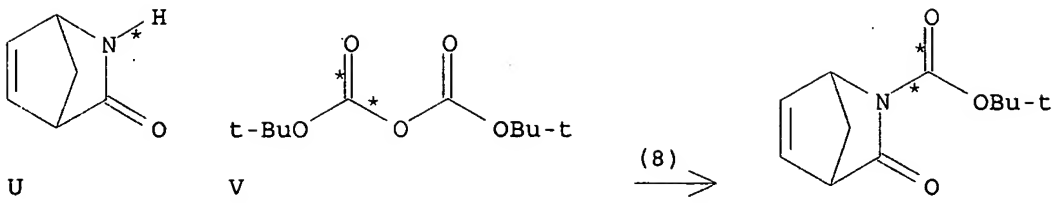
(7)



G
YIELD 26%

RX(7) RCT Q 10310-21-1, R 126261-74-3
RGT S 584-08-7 K2CO3
PRO G 175776-29-1
SOL 68-12-2 DMF

RX(8) OF 99 U + V ===> W...



U V (8) W

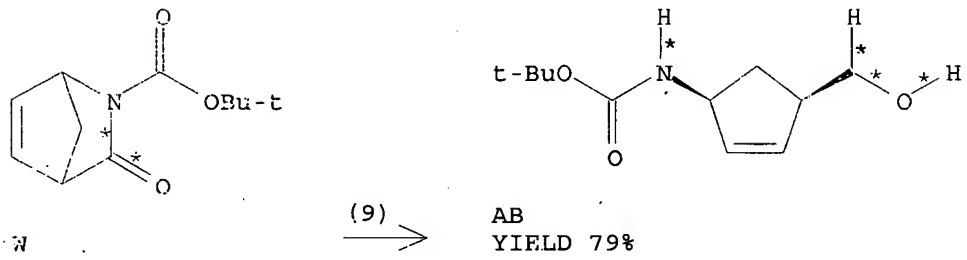
YIELD 99%

RX(8) RCT U 49805-30-3, V 24424-99-5

STAGE(1)
RGT X 121-44-8 Et3N
CAT 1122-58-3 4-DMAP
SOL 75-09-2 CH2Cl2

STAGE(2)
RGT D 7732-18-5 Water
SOL 60-29-7 Et2O, 7732-18-5 Water
PRO W 162427-15-8

RX(9) OF 99 ...W ===> AB...

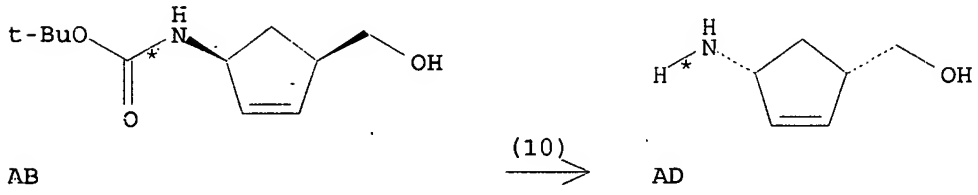


W (9) AB

YIELD 79%

RX(9) RCT W 162427-15-8
RGT AC 16940-66-2 NaBH4
PRO AB 153064-91-6
SOL 67-56-1 MeOH
NTE stereoselective

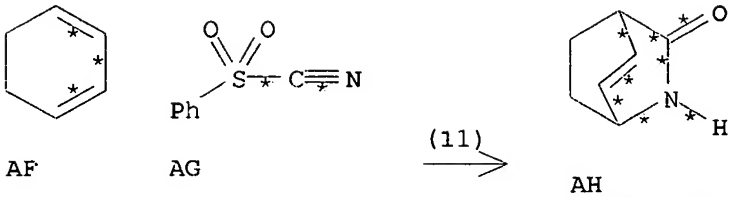
RX(10) OF 99 ...AB ===> AD



AB (10) AD

RX(10) RCT AB 153064-91-6
RGT AE 76-05-1 F3CCO2H
PRO AD 122624-72-0

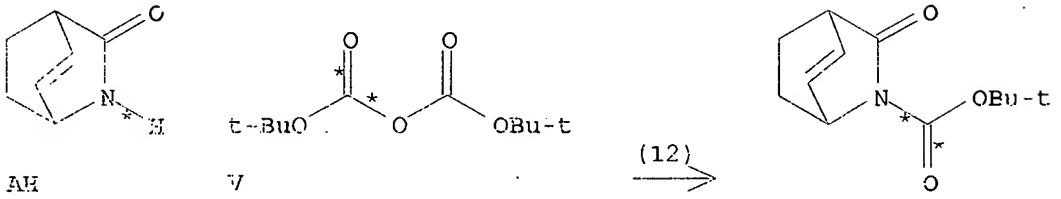
RX(11) OF 99  AF + AG ===> AH...




AF  AG  AH
YIELD 43%

RX(11)  RCT AF 592-57-4, AG 24224-99-5
PRO AH 39170-54-2
SOL 67-66-3 CHCl3

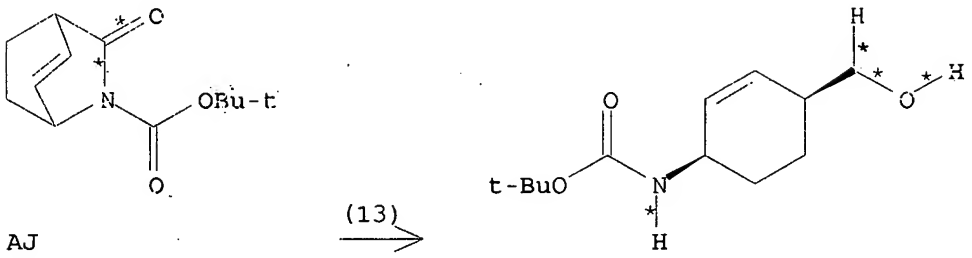
RX(12) OF 99  ...AH + V ===> AJ...




AH  V  AJ
YIELD 97%

RX(12)  RCT AH 39170-54-2, V 24424-99-5
RGT X 121-44-8 Et3N
PRO AJ 175651-10-2
CAT 1122-58-3 4-DMAP
SOL 75-09-2 CH2Cl2

RX(13) OF 99  ...AJ ===> AK...

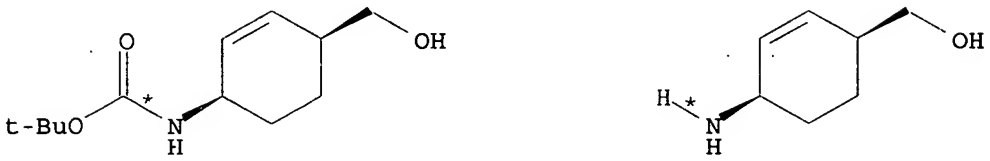



AJ  AK
YIELD 98%

RX(13)  RCT AJ 175651-10-2
RGT AC 16940-66-2 NaBH4
PRO AK 175651-11-3

SOL 67-56-1 MeOH
NTE stereoselective, stereoselective

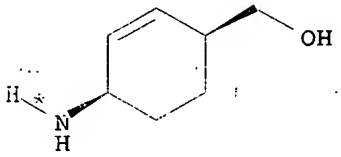
RX(14) OF 99 ...AK ===> AL...



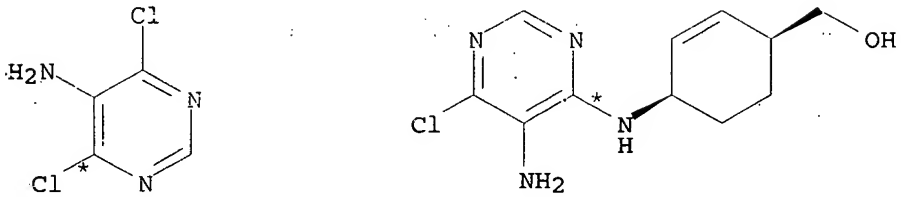
AK (14) AL

RX(14) RCT AK 175651-11-3
RGT AE 76-05-1 F3CCO2H
PRO AL 175651-12-4

RX(15) OF 99 ...AL + AM ===> AN...



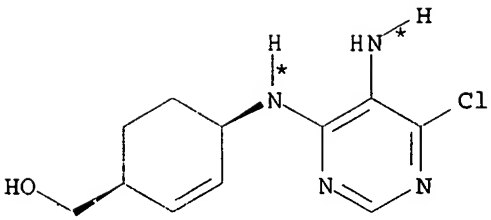
AL



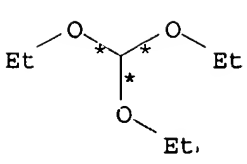
AM (15) AN
YIELD 50%

RX(15) RCT AL 175651-12-4, AM 5413-85-4
RGT AO 7087-68-5 EtN(Pr-i)2
PRO AN 175651-13-5
SOL 71-36-3 BuOH

RX(16) OF 99 ...AN + AQ ===> M...

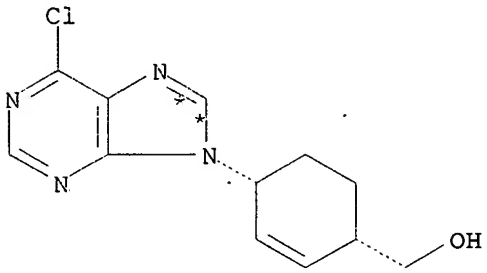


AN



AQ

(16)



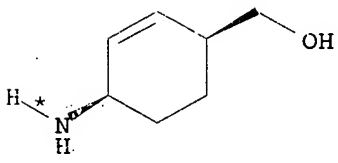
M
YIELD 95%

RX(16) RCT AN 175651-13-5, AQ 122-51-0

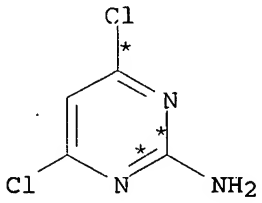
STAGE(1)
RGT AR 7647-01-0 HCl
SOL 122-51-0 CH(OEt)3, 7732-18-5 Water

STAGE(2)
RGT AS 1310-73-2 NaOH
SOL 7732-18-5 Water
PRO M 174466-13-8

RX(17) OF 99 ...AL + AT ===> AU...

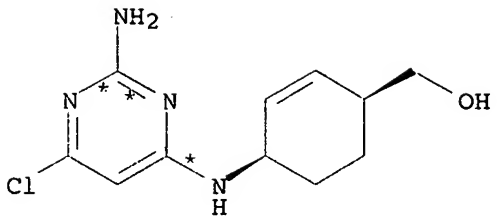


AL



AT

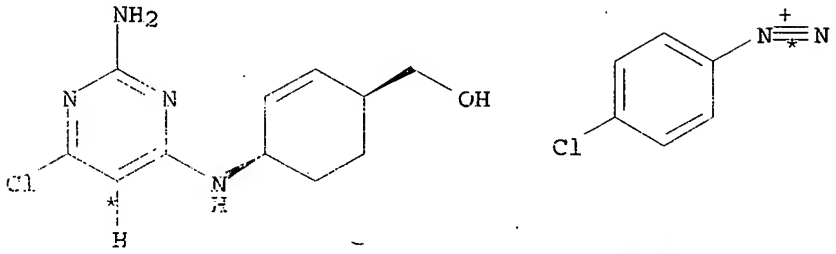
(17)



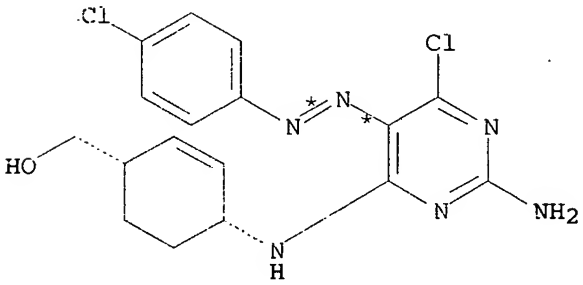
AU
YIELD 40%

RX(17) RCT AL 175651-12-4, AT 56-05-3
RGT X 121-44-8 Et3N
PRO AU 175651-14-6
SOL 64-17-5 EtOH

RX(18) OF 99 ...AU + AW ===> AX...



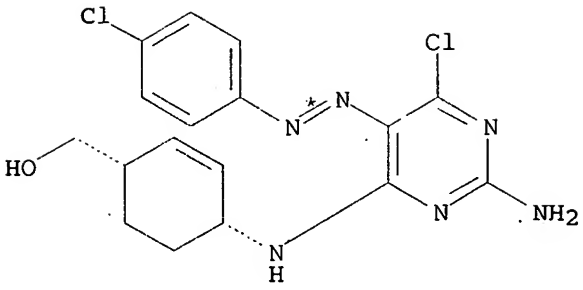
AU AW (18)



AX

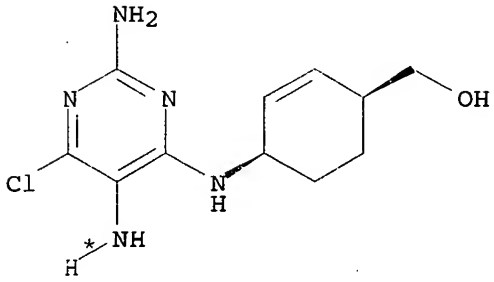
RX(18) RCT AU 175651-14-6, AW 2028-74-2
PRO AX 175651-15-7
SOL 67-56-1 MeOH, 7732-18-5 Water
NTE buffered soln. Acetate

RX(19) OF 99 ...AX ===> AY...



AX

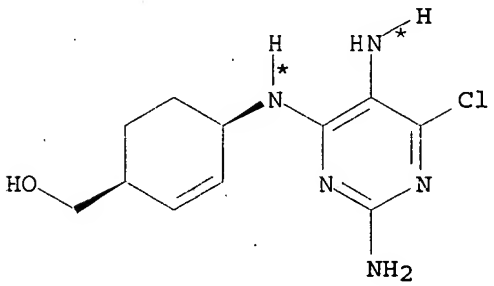
(19)



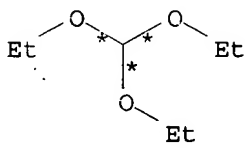
AY
YIELD 65%

RX(19) RCT AX 175651-15-7
RGT AZ 7440-66-6 Zn, BA 64-19-7 AcOH
PRO AY 175651-16-8
SOL 64-17-5 EtOH, 7732-18-5 Water

RX(20) OF 99 ...AY + AQ ===> O...

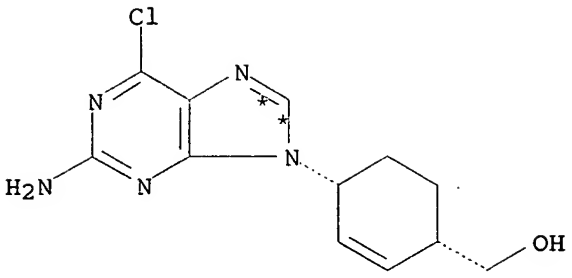


AY



AQ

(20)



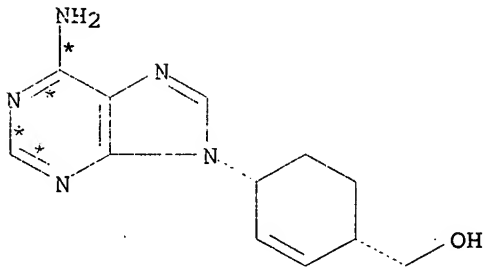
O
YIELD 61%

RX(20)  RCT  AY 175651-16-8, AQ 122-51-0

STAGE(1)
RGT  AR 7647-01-0 HCl
SOL  122-51-0 CH(OEt)3, 7732-18-5 Water

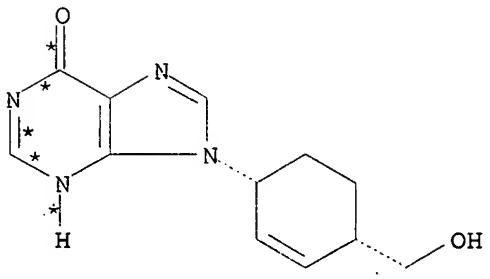
STAGE(2)
RGT  AS 1310-73-2 NaOH
SOL  7732-18-5 Water
PRO  O 174466-16-1

RX(21) OF 99  ...N  ===>  BB



N

(21)

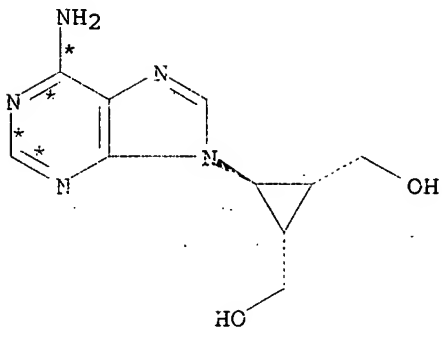


BB
YIELD 59%

RX(21)  RCT  N 174466-15-0

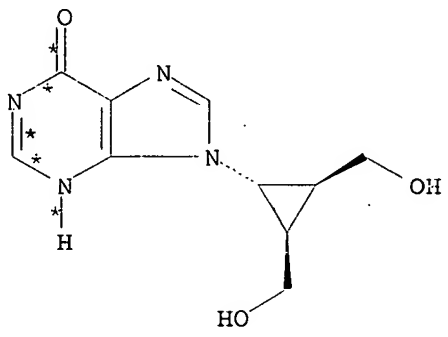
PRO BB 174466-14-9
CAT 9026-93-1 Adenosine deaminase
SOL 7732-18-5 Water
NTE buffered soln. Phosphate pH 7.0, biotransformation, enzymic, Adenosine deaminase type IV from calf intestinal mucosa used, alternative reaction conditions gave lower yield, high pressure, stereoselective

RX(22) OF 99 BC ===> BD



BC

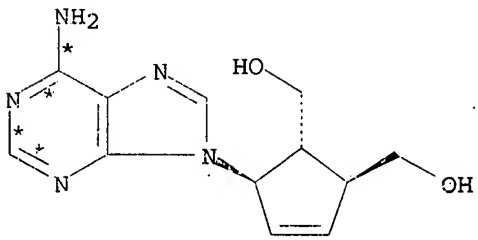
(22)



BD
YIELD 100%

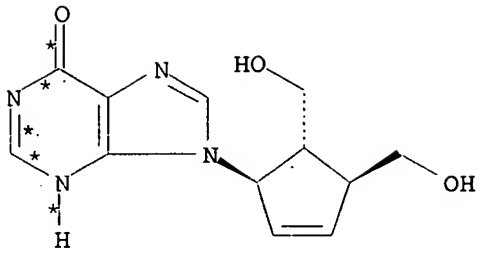
RX(22) RCT BC 132487-14-0
PRO BD 175776-30-4
CAT 9026-93-1 Adenosine deaminase
SOL 7732-18-5 Water
NTE buffered soln. Phosphate pH 7.0, biotransformation, enzymic, Adenosine deaminase type IV from calf intestinal mucosa used, alternative reaction conditions gave lower yield, high pressure, stereoselective

RX(23) OF 99 BE ===> BF



BE

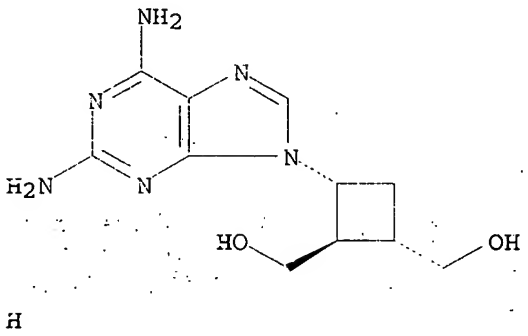
(23)



BF
YIELD 34%

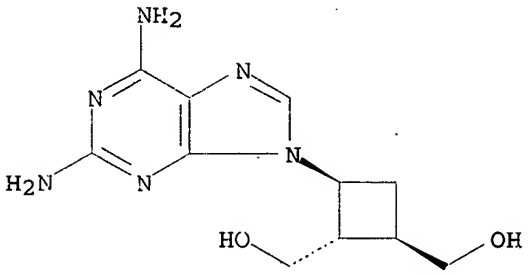
RX(23) RCT BE 140440-40-0
PRO BF 151896-53-6
CAT 9026-93-1 Adenosine deaminase
SOL 7732-18-5 Water
NTE buffered soln. Phosphate pH 7.0, biotransformation, enzymic, Adenosine deaminase type IV from calf intestinal mucosa used, high pressure, stereoselective

RX(24) OF 99 ...H ===> BG



H

(24)

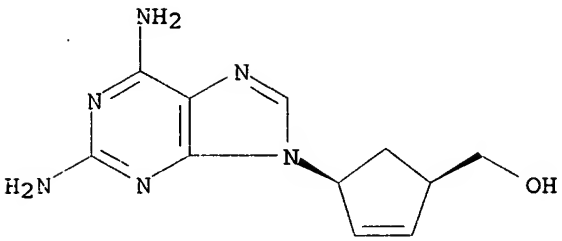


BG
YIELD 49%

RX(24) RCT H 129261-95-6
PRO BG 175776-32-6
CAT 9026-93-1 Adenosine deaminase
SOL 7732-18-5 Water
NTE buffered soln. Phosphate pH 7.0, biotransformation, enzymic, Adenosine deaminase type IV from calf intestinal mucosa used,

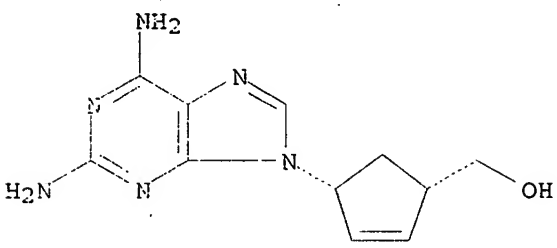
alternative reaction conditions gave lower yield,
stereoselective

RX(25) OF 99 BH ===> BI



BH

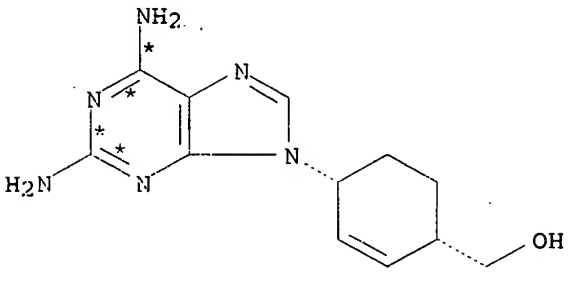
(25)



BI
YIELD 40%

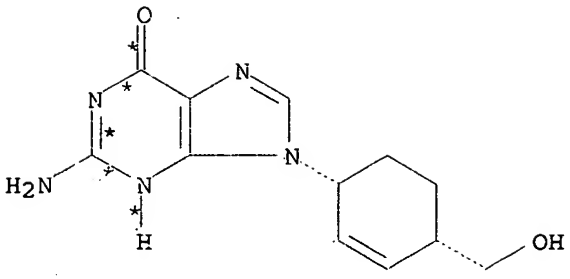
RX(25) RCT BH 118237-38-0
PRO BI 124752-25-6
CAT 9026-93-1 Adenosine deaminase
SOL 7732-18-5 Water
NTE buffered soln. Phosphate pH 7.0, biotransformation, enzymic,
Adenosine deaminase type IV from calf intestinal mucosa used,
alternative reaction conditions gave lower yield, high pressure,
stereoselective

RX(26) OF 99 ...P. ===> BJ



P

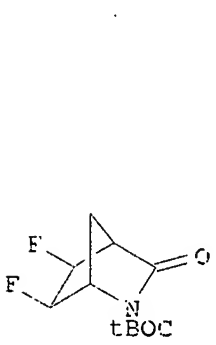
(26)



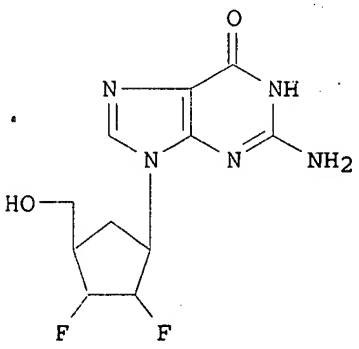
BJ
YIELD 33%

RX(26) RCT P 174466-18-3
PRO BJ 202530-27-6
CAT 9026-93-1 Adenosine deaminase
SOL 7732-18-5 Water
NTE buffered soln. Phosphate pH 7.0, biotransformation, enzymic, Adenosine deaminase type IV from calf intestinal mucosa used, alternative reaction conditions gave lower yield, high pressure, stereoselective

L2 ANSWER 116 OF 150 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 122:240292 CASREACT
TITLE: Synthesis of nucleotides and related compounds. Addition of molecular fluorine to bicyclo[2.2.1]hept-2-ene derivatives and conversion to fluorine-containing carbocyclic nucleosides
AUTHOR(S): Toyota, Akemi; Habutani, Chie; Katagiri, Nobuya; Kaneko, Chikara
CORPORATE SOURCE: Pharmaceutical Institute, Tohoku University, Sendai, 980, Japan
SOURCE: Tetrahedron Letters (1994), 35(31), 5665-8
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 33-9 (Carbohydrates)
GRAPHIC IMAGE:



I



II

ABSTRACT:
Stereoselective addition of mol. fluorine to bicyclo[2.2.1]hept-2-ene derivs. has been found to give exo,exo-difluoro adducts, e.g. I, in fair yields. I was

converted to the fluorine containing carbocyclic adenosine II and guanosine analogs.

SUPPL. TERM: carbocyclic dideoxydifluoro nucleoside; bicycloheptene stereoselective addn fluorination

INDEX TERM: Addition reaction
Fluorination
Stereochemistry
(stereoselective addition of bicycloheptene with fluorine in synthesis of fluorine-containing carbocyclic nucleosides)

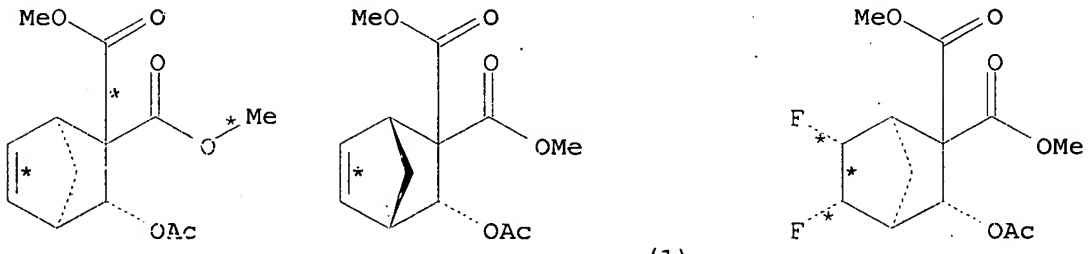
INDEX TERM: Nucleosides, preparation
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(stereoselective addition of bicycloheptene with fluorine in synthesis of fluorine-containing carbocyclic nucleosides)

INDEX TERM: 56-05-3, 2-Amino-4,6-dichloropyrimidine 694-98-4, Bicyclo[2.2.1]hept-5-en-2-one 2890-95-1 5257-37-4 5413-85-4, 5-Amino-4,6-dichloropyrimidine 17814-99-2 18317-73-2 20224-40-2 49805-30-3, 2-Azabicyclo[2.2.1]hept-5-en-3-one 109748-51-8 109748-52-9 162307-09-7 162427-15-8
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(stereoselective addition of bicycloheptene with fluorine in synthesis of fluorine-containing carbocyclic nucleosides)

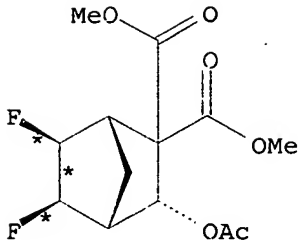
INDEX TERM: 162307-12-2P 162307-16-6P 162307-17-7P 162307-20-2P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(stereoselective addition of bicycloheptene with fluorine in synthesis of fluorine-containing carbocyclic nucleosides)

INDEX TERM: 162307-03-1P 162307-04-2P 162307-05-3P 162307-06-4P 162307-07-5P 162307-08-6P 162307-10-0P 162307-11-1P 162307-13-3P 162307-14-4P 162307-15-5P 162307-18-8P 162307-19-9P 162307-21-3P 162427-11-4P 162427-12-5P 162427-13-6P 162427-14-7P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(stereoselective addition of bicycloheptene with fluorine in synthesis of fluorine-containing carbocyclic nucleosides)

RX(1) OF 25 2 A + 2 B ===> C + D + E + F




2 A 2 B C



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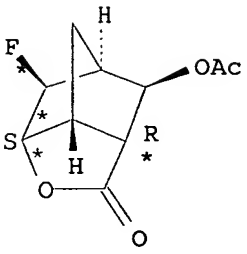
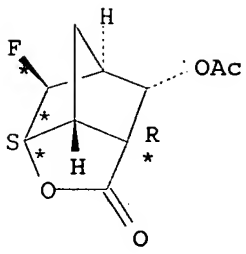


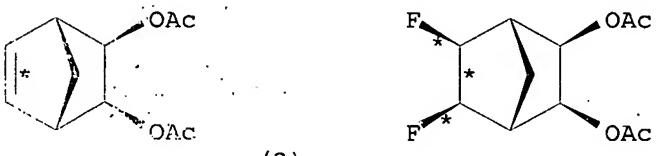
E



F

RX(1) RCT A 109748-52-9, B 109748-51-8
RGT G 7782-41-4 F2, H 7727-37-9 N2
PRO C 162307-03-1, D 162427-11-4, E 162307-04-2, F 162427-12-5
SOL 75-69-4 CFCl3, 67-66-3 CHCl3, 64-17-5 EtOH
NTE fluorine:nitrogen=5:95, 1:1 exo:endo for starting compounds, 72% overall yield, stereoselective

RX(2) OF 25 L ===> M



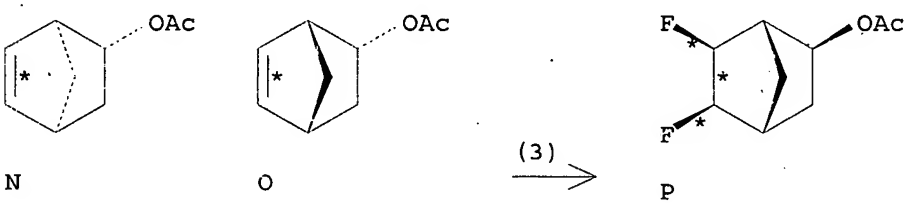
L

(2)

M
YIELD 40%

RX(2) RCT L 20224-40-2
RGT G 7782-41-4 F2, H 7727-37-9 N2
PRO M 162307-05-3
SOL 75-69-4 CFCl3, 67-66-3 CHCl3, 64-17-5 EtOH
NTE fluorine:nitrogen=5:95, stereoselective

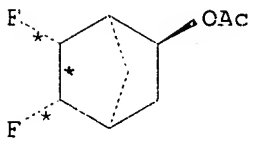
RX(3) OF 25 N + O ===> P + Q



N O

(3)

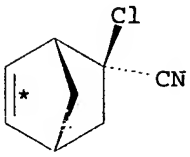
P



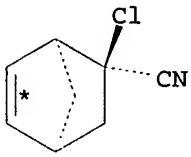
Q

RX(3)  RCT  N 5257-37-4, O 2890-95-1
       RGT  G 7782-41-4 F2, H 7727-37-9 N2
       PRO  P 162307-06-4, Q 162427-13-6
       SOL  75-69-4 CFCl3, 67-66-3 CHCl3, 64-17-5 EtOH
       NTE  stereoselective, fluorine:nitrogen=5:95, 1:4 exo:endo for starting compounds, 23% overall yield

RX(4) OF 25  R + S ===> T + U

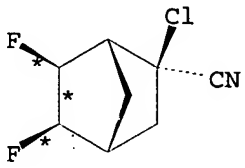



R

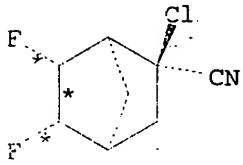



S

(4)



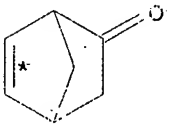

T




U

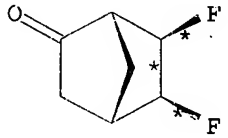
RX(4)  RCT  R 17814-99-2, S 18317-73-2
       RGT  G 7782-41-4 F2, H 7727-37-9 N2
       PRO  T 162307-07-5, U 162427-14-7
       SOL  75-69-4 CFCl3, 67-66-3 CHCl3, 64-17-5 EtOH
       NTE  stereoselective, fluorine:nitrogen=5:95, 1:6 exo:endo for starting compounds, 52% overall yield

RX(5) OF 25  V ===> W




V

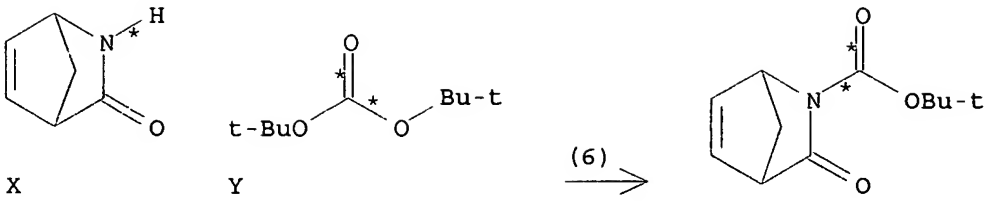
(5)




W
YIELD 30%

RX(5)  RCT  V 694-98-4
       RGT  G 7782-41-4 F2, H 7727-37-9 N2
       PRO  W 162307-08-6
       SOL  75-69-4 CFCl3, 67-66-3 CHCl3, 64-17-5 EtOH
       NTE  fluorine:nitrogen=5:95, stereoselective

RX(6) OF 25  X + Y ===> Z...

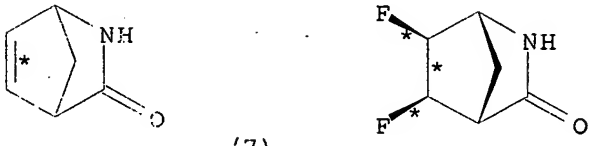



X Y (6) Z

YIELD 100%

RX(6) RCT X 49805-30-3, Y 34619-03-9
PRO Z 162427-15-8
NTE no solvent

RX(7) OF 25 X ===> AA

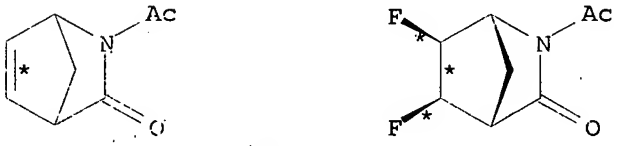



X (7) AA

YIELD 35%

RX(7) RCT X 49805-30-3
RGT G 7782-41-4 F2, H 7727-37-9 N2
PRO AA 162307-10-0
SOL 75-69-4 CFCl3, 67-66-3 CHCl3, 64-17-5 EtOH
NTE fluorine:nitrogen=5:95, stereoselective

RX(8) OF 25 AB ===> AC

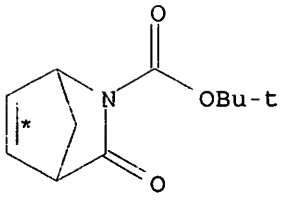



AB (8) AC

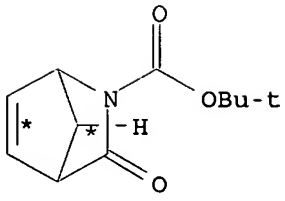
YIELD 40%

RX(8) RCT AB 162307-09-7
RGT G 7782-41-4 F2, H 7727-37-9 N2
PRO AC 162307-11-1
SOL 75-69-4 CFCl3, 67-66-3 CHCl3, 64-17-5 EtOH
NTE fluorine:nitrogen=5:95, stereoselective

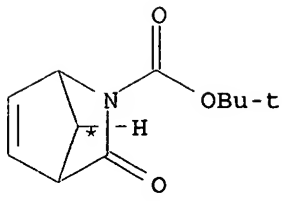
RX(9) OF 25 ...4 Z ===> AD + AE + AF + AG...



2 Z

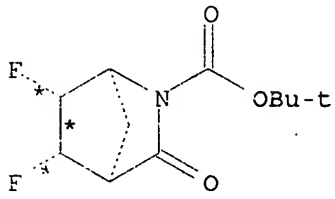


Z

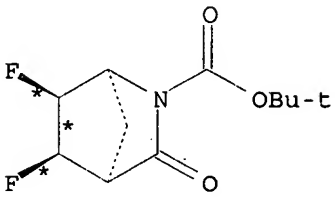


Z

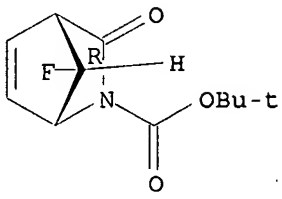
(9)



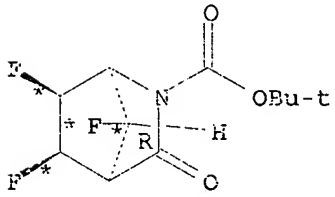
AD
YIELD 43%



AE
YIELD 5%



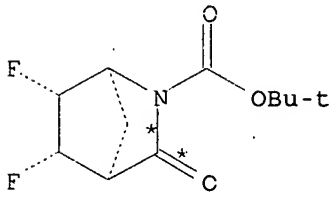
AF
YIELD 2%



AG
YIELD 4%

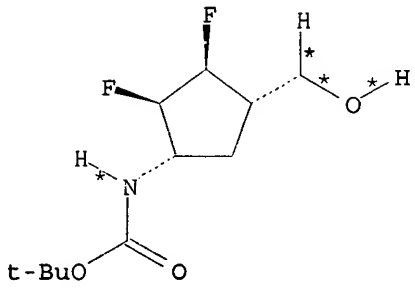
RX(9) RCT Z 162427-15-8
RGT G 7782-41-4 F2, H 7727-37-9 N2
PRO AD 162307-12-2, AE 162307-13-3, AF 162307-14-4, AG 162307-15-5
SOL 75-69-4 CFCl3, 67-66-3 CHCl3, 64-17-5 EtOH
NTE fluorine:nitrogen=5:95

RX(10) OF 25 ...AD ===> AH...



AD

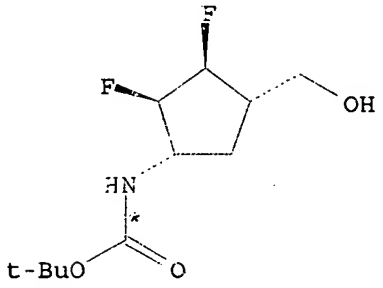
(10)



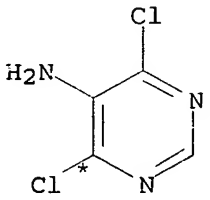
AH
YIELD 84%

RX(10) RCT AD 162307-12-2
RGT AI 16940-66-2 NaBH4
PRO AH 162307-16-6
SOL 67-56-1 MeOH
NTE stereoselective

RX(11) OF 25 ...**AH** + **AK** ===> **AL**...

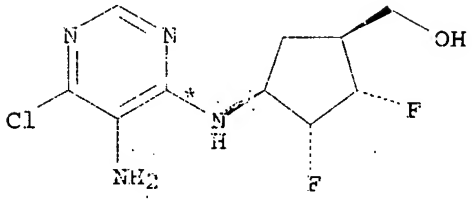


AH



AK

(11) →



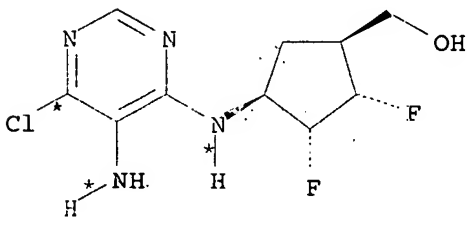
AL
YIELD 40%

RX(11) RCT AH **162307-16-6**

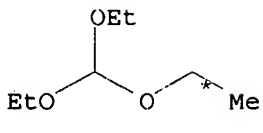
STAGE(1)
RGT AM 76-05-1 F3CCO2H
SOL 7732-18-5 Water

STAGE(2)
RCT AK **5413-85-4**
RGT AN 7087-68-5 EtN(Pr-i)2
SOL 71-36-3 BuOH
PRO AL **162307-18-8**

RX(12) OF 25 ...AL + AQ ===> AR

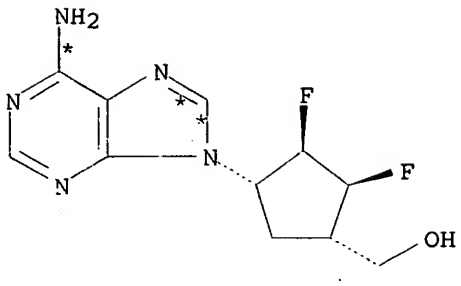


AL



AQ

(12) →



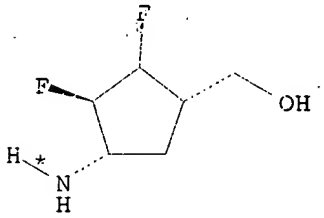
AR
YIELD 49%

RX(12) RCT AL 162307-18-8, AQ 122-51-0

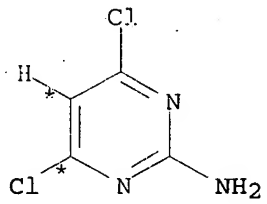
STAGE(1)
RGT AS 7647-01-0 HCl
SOL 7732-18-5 Water

STAGE(2)
RGT AT 7664-41-7 NH3
SOL 67-56-1 MeOH
PRO AR 162307-19-9

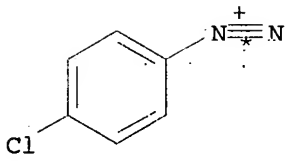
RX(13) OF 25 AU + AV + AW ===> AX...



AU



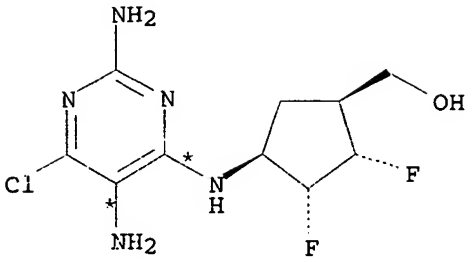
AV



● $Cl^-$

AW

(13)



AX
YIELD 32%

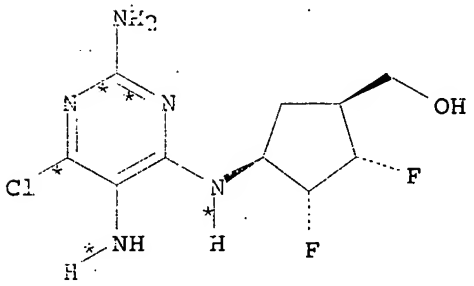
RX(13) RCT AU 162307-17-7, AV 56-05-3

STAGE(1)

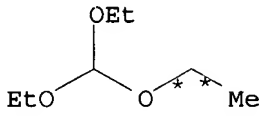
STAGE(2)
RCT AW 2028-74-2
RGT AY 64-19-7 AcOH, AZ 127-09-3 AcONa
SOL 7732-18-5 Water

STAGE(3)
RGT BA 7440-66-6 Zn, AY 64-19-7 AcOH
SOL 64-17-5 EtOH, 7732-18-5 Water
PRO AX 162307-20-2

RX(14) OF 25 ...AX + AQ ===> BB

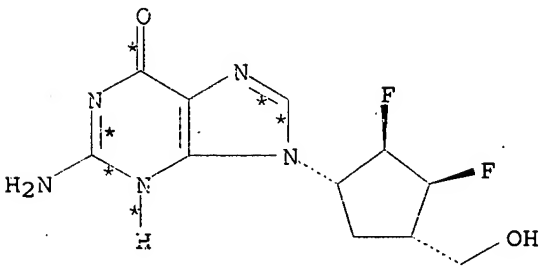


AX



AQ

(14)



BB
YIELD 53%

RX(14) RCT AX 162307-20-2, AQ 122-51-0

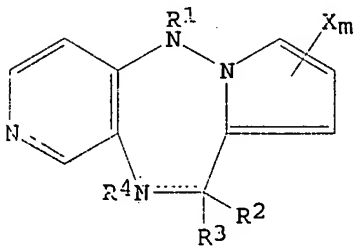
STAGE(1)
RGT AS 7647-01-0 HCl
SOL 7732-18-5 Water

STAGE(2)
RGT AS 7647-01-0 HCl
SOL 7732-18-5 Water
PRO BB 162307-21-3

L2 ANSWER 136 OF 150 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 112:216978 CASREACT
TITLE: Preparation of pyrido[3,4-f]pyrrolo[1,2-b][1,2,5]triazepines as drugs
INVENTOR(S): Effland, Richard C.; Davis, Larry; Kapples, Kevin J.; Olsen, Gordon E.
PATENT ASSIGNEE(S): Hoechst-Roussel Pharmaceuticals, Inc., USA
SOURCE: U.S., 14 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C07D471-14
US PATENT CLASSIF.: 540554000
CLASSIFICATION: 28-22 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 4879382 | A | 19891107 | US 1988-223847 | 19880725 |
| EP 352629 | A2 | 19900131 | EP 1989-113301 | 19890720 |
| EP 352629 | A3 | 19910703 | | |
| R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| DK 8903645 | A | 19900126 | DK 1989-3645 | 19890724 |
| JP 02073085 | A2 | 19900313 | JP 1989-189009 | 19890724 |
| US 4914103 | A | 19900403 | US 1989-397922 | 19890824 |
| US 4996205 | A | 19910226 | US 1990-468402 | 19900119 |
| PRIORITY APPLN. INFO.: | | | US 1988-223847 | 19880725 |
| | | | US 1989-397922 | 19890824 |

OTHER SOURCE(S): MARPAT 112:216978
GRAPHIC IMAGE:




I

ABSTRACT:
Title compds. I (R1 = alkyl, arylalkyl, aminoalkyl; R2 = H, alkyl, arylalkyl,

aminoalkyl, heterocyclyl; R3 = H, alkyl; R2R3 = O; R4 = H, alkyl, arylalkyl, aminoalkyl, HCO, alkylcarbonyl, aminocarbonyl, arylaminocarbonyl, heterocyclyl; X = halo, alkyl, alkenyl, HCO, alkanol; m = 0, 1) useful as antidepressants, analgesics, inflammation inhibitors, and memory enhancers, are prepared 5-Methyl-5H-pyrido[3,4-f]pyrrolo[1,2-b][1,2,5]triazepine (preparation given) in EtOH was treated with NaBH4 to give I (R1 = Me, R2 = R3 = R4 = H; Xm = 0) (II). In a test for analgesic activity II showed 50% inhibition of writhing at 12 mg/kg, s.c. Tests for conducted also for inflammation inhibition, antidepressant activity and memory enhancement.

SUPPL. TERM: pyridopyrrolotriazepine prepn drug; analgesic
pyridopyrrolotriazepine prepn; antiinflammatory
pyridopyrrolotriazepine prepn; antidepressant
pyridopyrrolotriazepine prepn; memory enhancer
pyridopyrrolotriazepine prepn

INDEX TERM: Memory, biological
(enhancement of, pyridopyrrolotriazepines for)

INDEX TERM: Analgesics
Antidepressants
Inflammation inhibitors
(pyridopyrrolotriazepines)

INDEX TERM: 100-58-3, Phenylmagnesium bromide 103-63-9 104-77-8
109-54-6, (Dimethylaminopropyl chloride 917-64-6,
Methylmagnesium iodide 5570-77-4
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(Grignard reaction of, with methylpyridopyrrolotriazepine
)

INDEX TERM: 541-41-3, Ethyl chloroformate
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(acylation by, of aminopyrrole)

INDEX TERM: 765-39-9, N-Amino pyrrole
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(acylation of)

INDEX TERM: 30525-89-4, Paraformaldehyde
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with (methoxyphenyl)piperazine and
pyridolepyrrolotriazepine derivative)

INDEX TERM: 35386-24-4
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with paraformaldehyde and
pyridolepyrrolotriazepine derivative)

INDEX TERM: 64-18-6, Formic acid, reactions
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(formylation by, of pyridolepyrrolotriazepine derivs.)

INDEX TERM: 110956-01-9P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and acylation of)

INDEX TERM: 126738-24-7P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(preparation and condensation with paraformaldehyde and
piperazine derivative)

INDEX TERM: 111225-54-8P 126738-23-6P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of)

INDEX TERM: 126738-05-4P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(preparation and hydrolysis)

INDEX TERM: 126738-04-3P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and methylation of)

INDEX TERM: 110955-68-5P 126738-06-5P

ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reactions of)

INDEX TERM: 110955-69-6P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(preparation and substitution with chloronitropyridine)

INDEX TERM: 110955-67-4P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

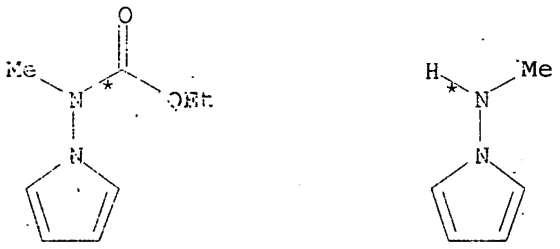
INDEX TERM: 126738-07-6P 126738-08-7P 126738-09-8P 126738-10-1P
126738-11-2P 126738-12-3P 126738-13-4P 126738-14-5P
126738-15-6P 126738-16-7P 126738-17-8P 126738-18-9P
126738-20-3P 126738-21-4P 126738-22-5P
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as drug)

INDEX TERM: 106-96-7, Propargyl bromide
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(propargylation by, of pyridylpyrrolotriazepine derivs.)

INDEX TERM: 126738-19-0
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reduction of)

INDEX TERM: 13091-23-1, 4-Chloro-3-nitropyridine
ROLE: PROC (Process)
(substitution of, with (methylamino)pyrrole)

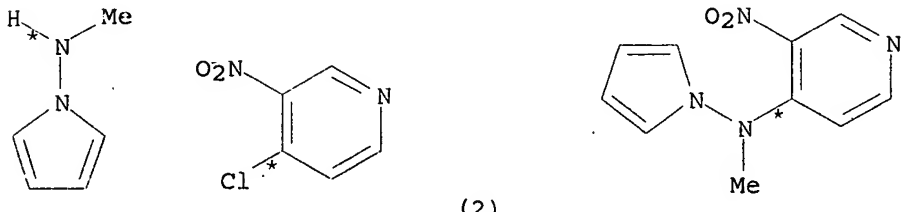
RX(1) OF 157 ...A ===> B...



A (1) B

RX(1) RCT A 126738-05-4
PRO B 110955-69-6

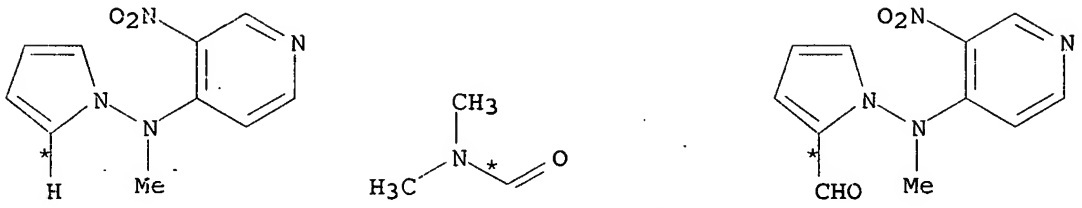
RX(2) OF 157 ...B + C ===> D...



B C (2) D
YIELD 78%

RX(2) RCT B 110955-69-6, C 13091-23-1
PRO D 110955-68-5

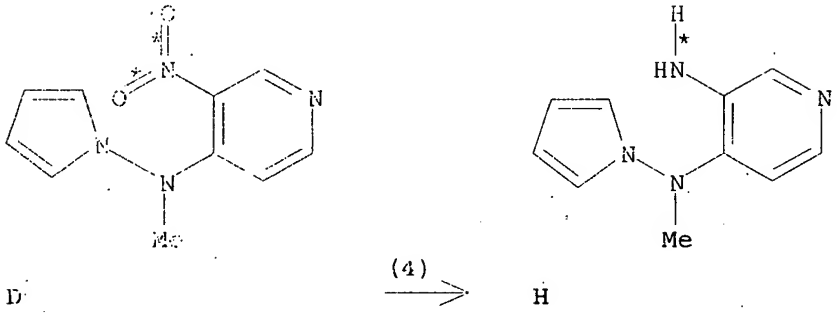
RX(3) OF 157 ...D + E ===> F...




D E F

RX(3) RCT D 110955-68-5, E 68-12-2
RGT G 10025-87-3 POCl3
PRO F 111225-54-8

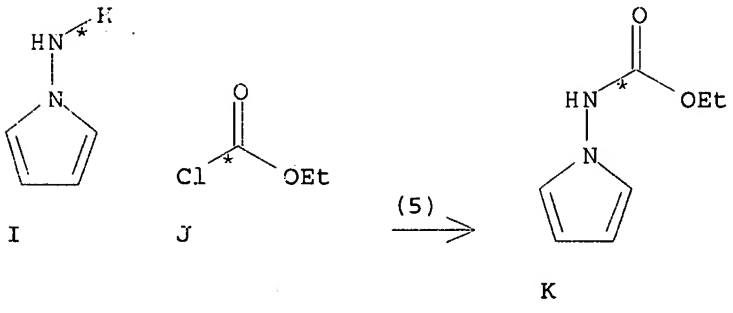
RX(4) OF 157 ...D ===> H...




D H

RX(4) RCT D 110955-68-5
PRO H 110956-01-9

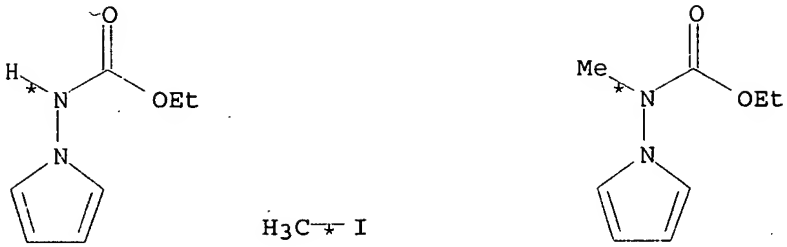
RX(5) OF 157 ...I + J ===> K...




I J K

RX(5) RCT I 765-39-9, J 541-41-3
PRO K 126738-04-3

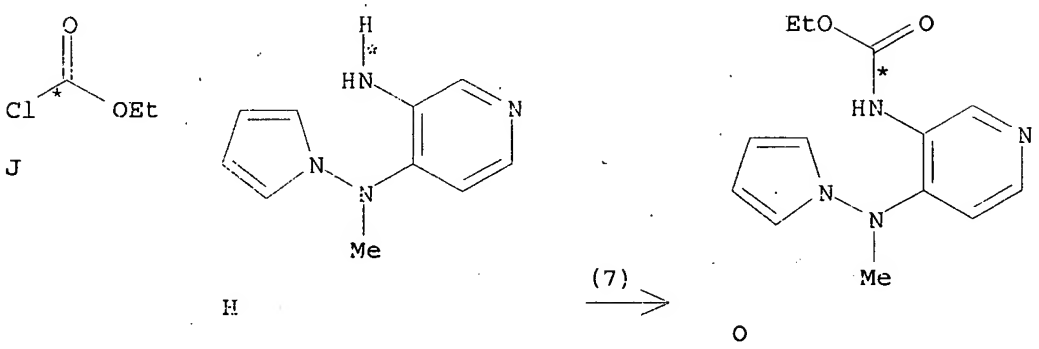
RX(6) OF 157 ...K + L ===> A...



K L (6) A

RX(6) RCT K 126738-04-3, L 74-88-4
PRO A 126738-05-4
CAT 865-47-4 t-BuOK
SOL 109-99-9 THF

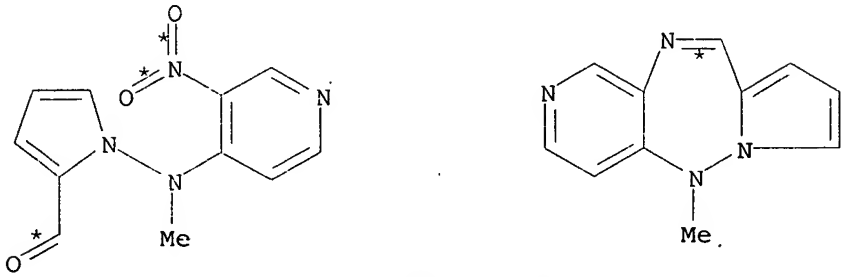
RX(7) OF 157 ...J + H ===> O



J H (7) O

RX(7) RCT J 541-41-3, H 110956-01-9
PRO O 126738-23-6

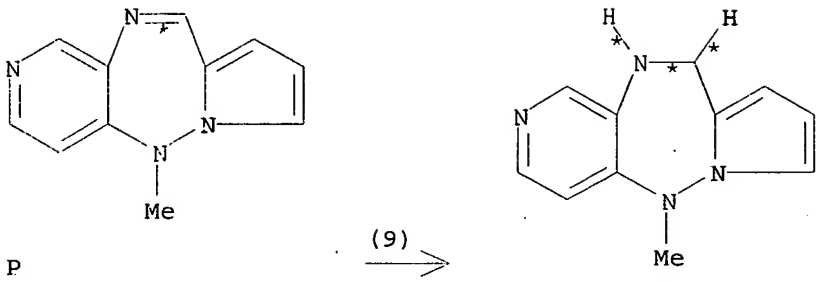
RX(8) OF 157 ...F ===> P...



F (8) P
YIELD 38%

RX(8) RCT F 111225-54-8
PRO P 126738-06-5

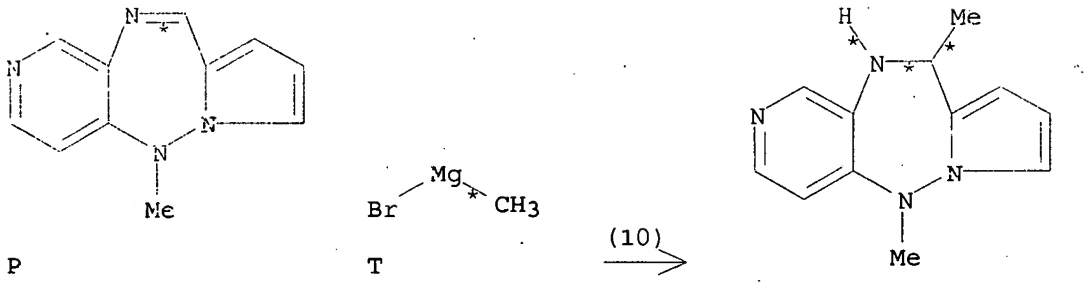
RX(9) OF 157 ...P ===> Q...




P Q

RX(9) RCT P 126738-06-5
PRO Q 126738-07-6
CAT 16940-66-2 NaBH4, 13755-29-8 Na[BF4]

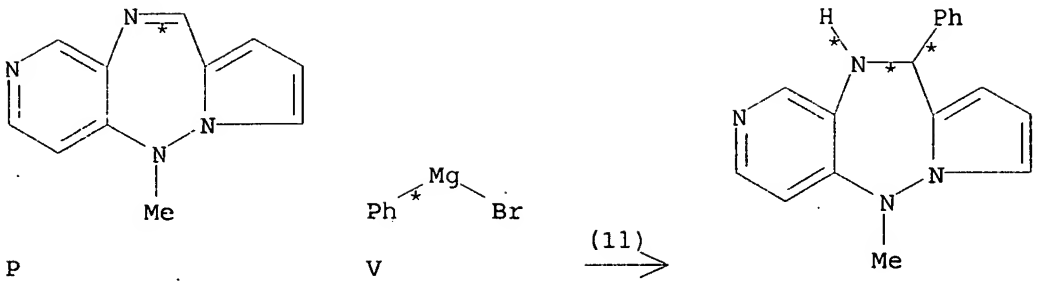
RX(10) OF 157 ...P + T ===> U




P T U
YIELD 48%

RX(10) RCT P 126738-06-5, T 75-16-1
PRO U 126738-08-7

RX(11) OF 157 ...P + V ===> W

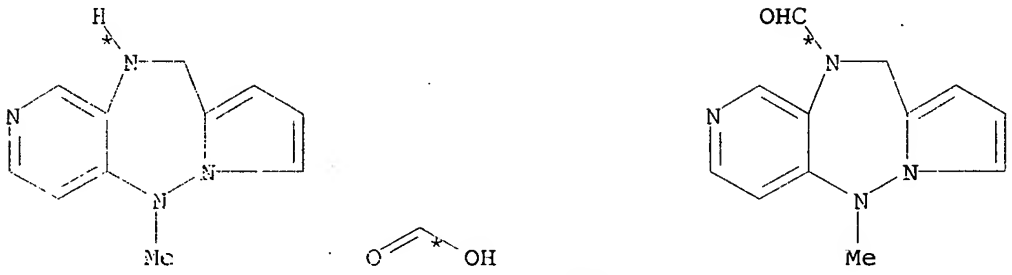


P V (11) W

W
YIELD 64%

RX(11) RCT P 126738-06-5, V 100-58-3
PRO W 126738-09-8

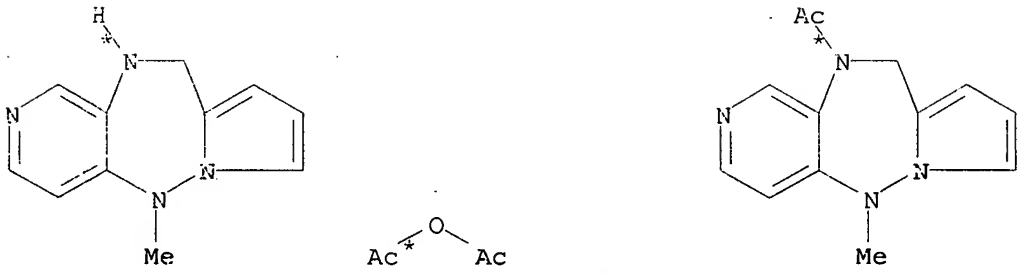
RX(12) OF 157 ...Q + X ===> Y



Q X (12) Y

RX(12) RCT Q 126738-07-6, X 64-18-6
PRO Y 126738-21-4

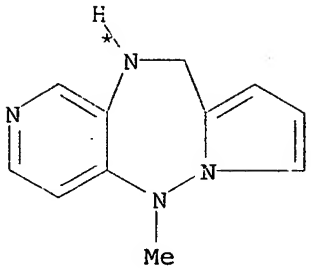
RX(13) OF 157 ...Q + Z ===> AA



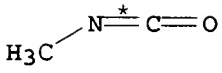
Q Z (13) AA

RX(13) RCT Q 126738-07-6, Z 108-24-7
PRO AA 126738-12-3

RX(14) OF 157 ...Q + AB ===> AC

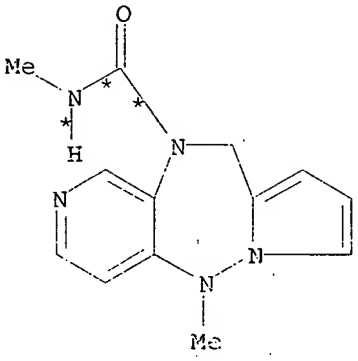


Q



AB

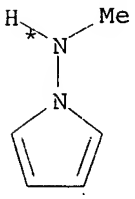
(14)



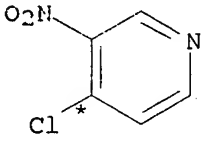
AC

RX(14) RCT Q 126738-07-6, AB 624-83-9
PRO AC 126738-14-5

RX(15) OF 157 B + C ===> D

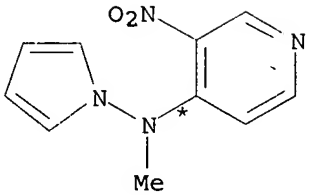


B



C

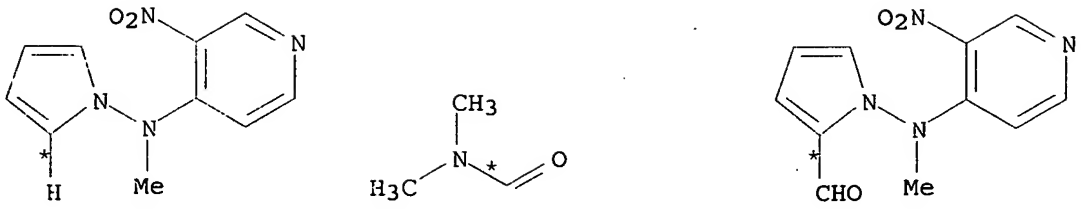
(15)



D

RX(15) RCT B 110955-69-6, C 13091-23-1
PRO D 110955-68-5
SOL 68-12-2 DMF

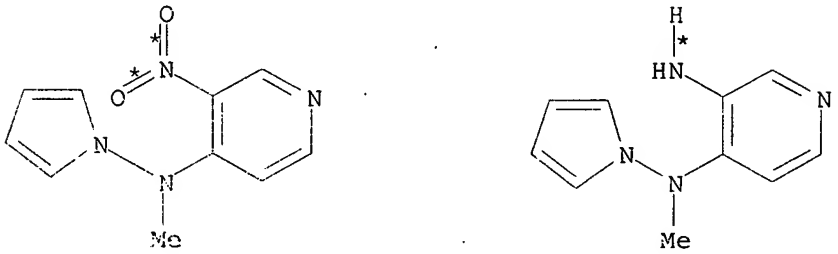
RX(16) OF 157 D + E ===> F



D E (16) F

RX(16) RCT D 110955-68-5, E 68-12-2
RGT G 10025-87-3 POCl3
PRO F 111225-54-8
SOL 68-12-2 DMF, 107-06-2 ClCH2CH2Cl

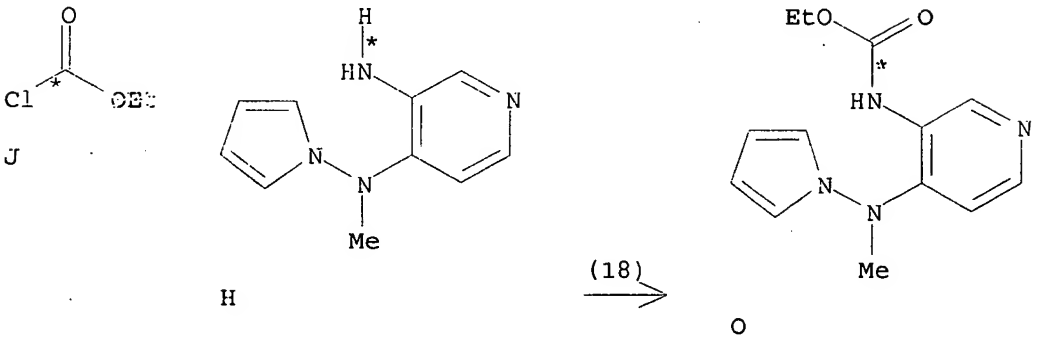
RX(17) OF 157 D ===> H



D (17) H

RX(17) RCT D 110955-68-5
PRO H 110956-01-9
SOL 67-56-1 MeOH

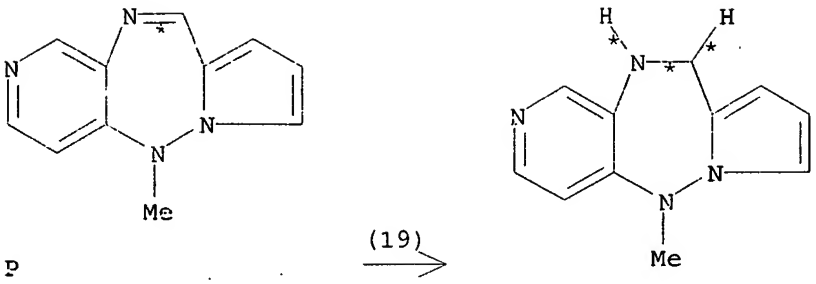
RX(18) OF 157 J + H ===> O



J H (18) O

RX(18) RCT J 541-41-3, H 110956-01-9
PRO O 126738-23-6
SOL 75-09-2 CH2Cl2

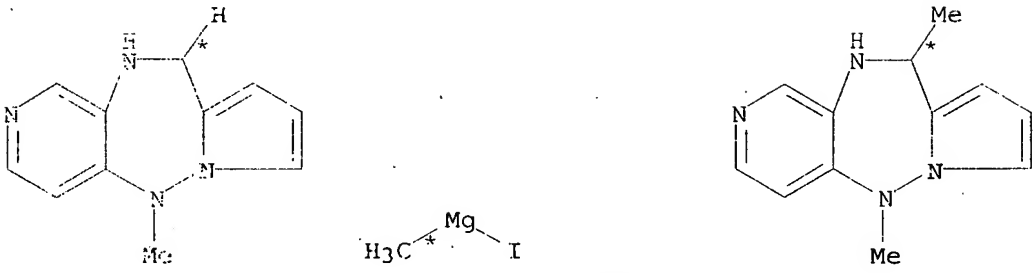
RX(19) OF 157 P ===> Q



P (19) Q

RX(19) RCT P 126738-06-5
RGT R 16940-66-2 NaBH4
PRO Q 126738-07-6
SOL 64-17-5 EtOH

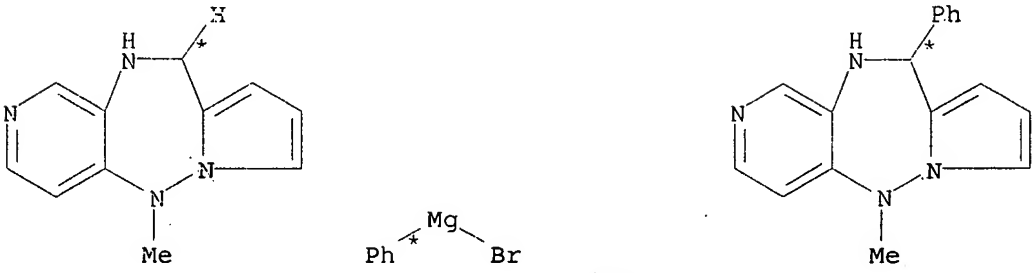
RX(20) OF 157 ...Q + AH ===> U



Q AH (20) U
YIELD 48%

RX(20) RCT Q 126738-07-6, AH 917-64-6
PRO U 126738-08-7

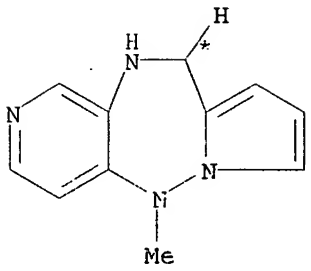
RX(21) OF 157 ...Q + V ===> W



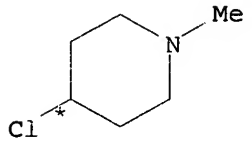
Q V (21) W
YIELD 64%

RX(21)  RCT  Q 126738-07-6, V 100-58-3
        PRO  W 126738-09-8

RX(22) OF 157  ...Q + AI ===> AJ

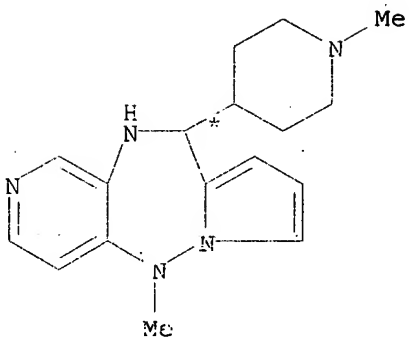


Q



AI

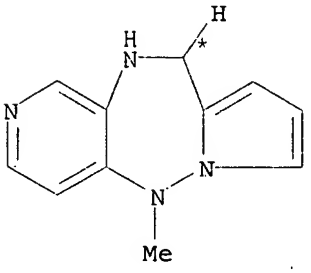
(22)



AJ

RX(22)  RCT  Q 126738-07-6, AI 5570-77-4
        PRO  AJ 126738-10-1
        SOL  109-99-9 THF

RX(23) OF 157  ...Q + AK ===> AL



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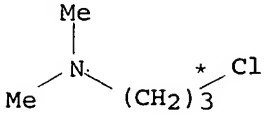
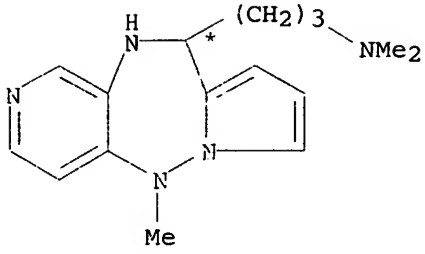


AK

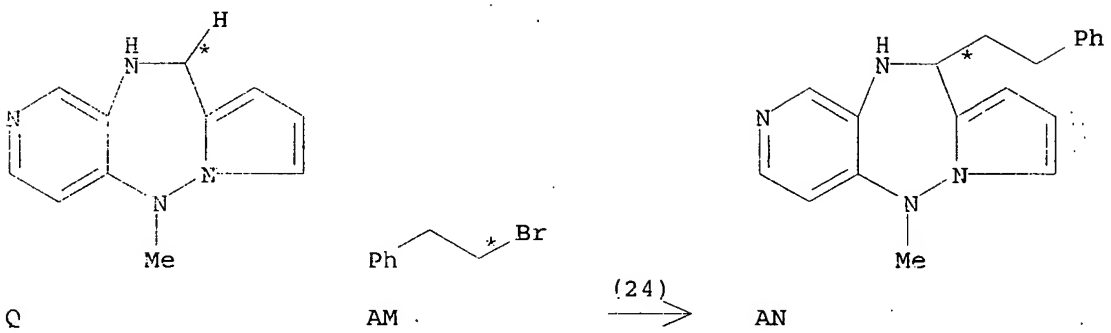
(23)



AL
YIELD 50%

RX(23) RCT Q 126738-07-6, AK 109-54-6
PRO AL 126738-11-2

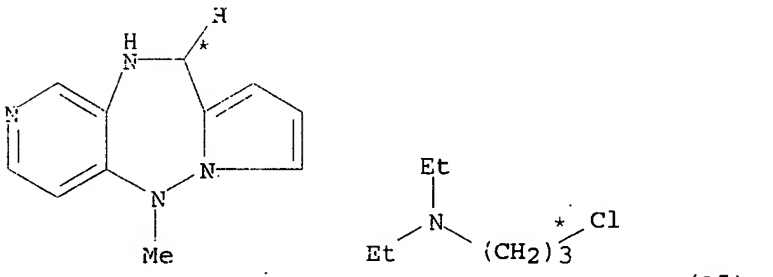
RX(24) OF 157 ...Q + AM ===> AN



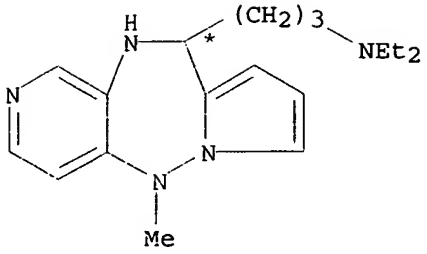
Q AM (24) AN

RX(24) RCT Q 126738-07-6, AM 103-63-9
PRO AN 126738-16-7
CAT 106-93-4 BrCH2CH2Br

RX(25) OF 157 ...Q + AP ===> AQ



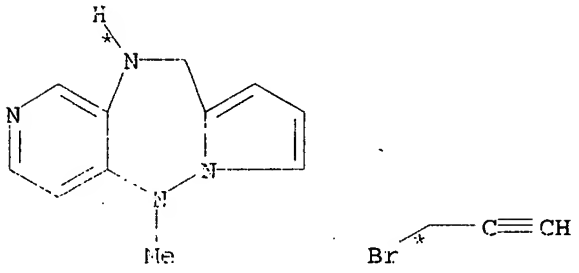
Q AP (25)



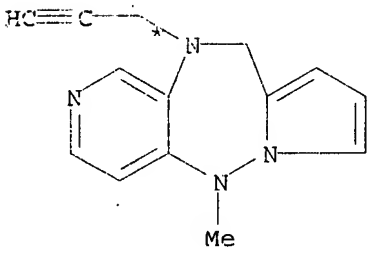
AQ

RX(25) RCT Q 126738-07-6, AP 104-77-8
PRO AQ 126738-17-8

RX(26) OF 157 ...Q + AR ===> AS...



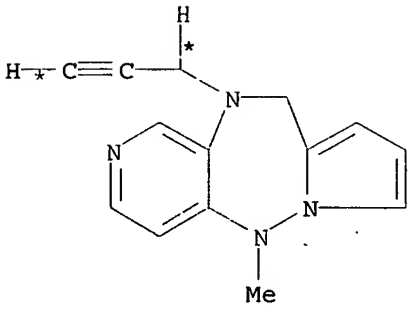
Q AR (26)



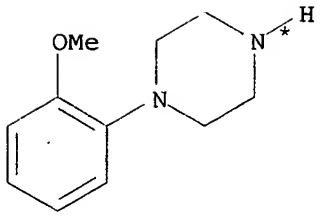
AS

RX(26) RCT Q 126738-07-6, AR 106-96-7
RGT AT 7646-69-7 NaH
PRO AS 126738-24-7
SOL 68-12-2 DMF

RX(27) OF 157 ...AS + AU ===> AV...



AS



AU

(27)

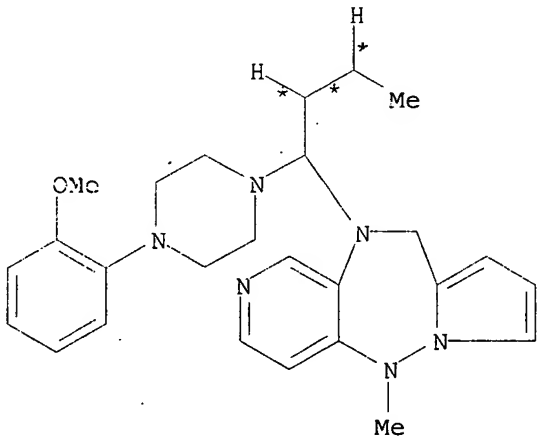
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(27) RCT AS 126738-24-7, AU 35386-24-4
PRO AV 126738-19-0

RX(28) OF 157 ...AV ===> AW

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

(28)



AW

RX(28) RCT AV 126738-19-0
PRO AW 126738-20-3
SOL 64-17-5 EtOH

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